U.S. Department of Health & Human Services

Food and Drug Administration

SAVE REQUEST

USER:	(jsh)
FOLDER:	K072741 - 650 pages
COMPANY:	INGFERTILITY, LLC (INGFERTILITY)
PRODUCT:	LUBRICANT, PATIENT, VAGINAL, LATEX COMPATIBLE (NUC)
SUMMARY:	Product: PRE-VA VAGINAL LUBRICANT
DATE REQUESTED:	Nov 2, 2011
DATE PRINTED:	Nov 2, 2011
Note:	Printed

K072741

510(k) Summary
Pre~Va Vaginal Lubricant

JUL 16 2008

I. General Information on Submitter

Address:	INGfertility, LLC (Subsidiary of Bio-Origyn, LLC) 17206 S. Spangle Creek Rd. Valleyford, WA 99036 USA
Telephone:	509.443.0149
Fax:	509.471.9638
Email:	dclifton@ingfertility.com
Contact Person:	G. Dennis Clifton, Pharm.D.
Date Prepared:	March 18, 2008

II. General Information on Device

Proprietary Name:	Pre~Va Vaginal Lubricant
Classification Name:	lubricant, patient, vaginal, latex compatible (21 CFR 884.5300, Product Code NUC)

III. Predicate Devices

Predicate Device	510(k) control #
Pre' Vaginal Lubricant	K051436

IV. Description of Device

This product is a non-sterile, water-based personal lubricant formulated to supplement the body's own natural lubricating fluids. Pre~Va is used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. It is also used as a personal lubricant to supplement the body's own natural lubricating fluids and to enhance the comfort of intimate sexual activity. The formulation does not harm sperm function and has a pH and osmolarity that are physiologic ("balanced") to that of fertile cervical mucus and semen. The product is compatible with latex and polyurethane condoms. Following is the ingredient list for Pre~Va Vaginal Lubricant:

Ingredients
Water
Hydroxyethylcellulose, NF
Pluronic 127, NF
Sodium Chloride, USP
Arabinogalactan
Sodium Phosphate
Carbopol 934P, NF
Methyl Paraben, USP
Sodium Hydroxide, NF
Potassium Phosphate

V. Intended Use

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

VI. Technological Characteristics of Device Compared to Predicate Device
All of the technological characteristics of Pre~Va are identical to the predicate device.

VII. Summary of Performance Data
The performance data of Pre~Va are identical to the predicate.

VIII. Conclusion
Pre~Va Vaginal Lubricant is safe for its intended use and substantially equivalent to the predicate device Pre' Vaginal Lubricant.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 16 2008

Dennis Clifton, Pharm.D.
Vice President
INGfertility, LLC
17206 South Spangle Creek Road
VALLEYFORD WA 99036

Re: K072741
Trade/Device Name: Pre-Va Vaginal Lubricant
Regulatory Class: 21 CFR 884.5300
Regulation Number: Condom
Product Code: NUC
Dated: July 1, 2008
Received: July 8, 2008

Dear Dr. Clifton:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at one of the following numbers, based on the regulation number at the top of this letter.

21 CFR 876.xxxx	(Gastroenterology/Renal/Urology)	240-276-0115
21 CFR 884.xxxx	(Obstetrics/Gynecology)	240-276-0115
21 CFR 892.xxxx	(Radiology)	240-276-0120
Other		240-276-0100

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Nancy C Brogdon

Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K072741

Device Name: Pre~Va Vaginal Lubricant

Indications for Use:

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms

Prescription Use _____ AND/OR Over-The-Counter Use __X_____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K072741

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

JUL 16 2008

Dennis Clifton, Pharm.D.
Vice President
INGfertility, LLC
17206 South Spangle Creek Road
VALLEYFORD WA 99036

Re: K072741
Trade/Device Name: Pre-Va Vaginal Lubricant
Regulatory Class: 21 CFR 884.5300
Regulation Number: Condom
Product Code: NUC
Dated: July 1, 2008
Received: July 8, 2008

Dear Dr. Clifton:

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If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

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If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Center for Devices and Radiological Health's (CDRH's) Office of Compliance at one of the following numbers, based on the regulation number at the top of this letter.

21 CFR 876.xxxx	(Gastroenterology/Renal/Urology)	240-276-0115
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21 CFR 892.xxxx	(Radiology)	240-276-0120
Other		240-276-0100

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Sincerely yours,

Nancy C Brogdon

Nancy C. Brogdon
Director, Division of Reproductive,
Abdominal, and Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K072741

Device Name: Pre~Va Vaginal Lubricant

Indications for Use:

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms

Prescription Use _____ AND/OR Over-The-Counter Use __X_____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of Reproductive, Abdominal,
and Radiological Devices
510(k) Number K072741

Page __ of ___

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

June 10, 2008

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Device: PRE-VA VAGINAL LUBRICANT

Extended Until: 24-JUL-2008

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

INGfertility

June 3, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

RE: K072741
Pre~Va Vaginal Lubricant – extension request

Dear Sir/Madam:

The above referenced 510(k) submission has been extended until 24-June-2008. The testing currently being conducted will not be completed by that date. We respectfully request a further extension to complete this work and submit a response.

Please contact me if you have questions or need further information.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

K072

INGfertility, LLC
17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

May 12, 2008

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Device: PRE-VA VAGINAL LUBRICANT

Extended Until: 24-JUN-2008

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

INGfertility

May 5, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

FDA CDRH DMC

MAY 12 2008

Received

RE: K072741
Pre~Va Vaginal Lubricant – extension request

Dear Sir/Madam:

We have received the April 25, 2008 correspondence regarding the above referenced 510(k) submission. We will need greater than thirty days to gather the requested information. Therefore, the purpose of this letter is to officially request an extension of time to obtain the requested information and submit a response.

Please contact me if you have questions or need further information.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

INGfertility, LLC
17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

K7

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

APR 25 2008

INGfertility, LLC
c/o Dennis Clifton, Pharm.D.
Vice President
17206 South Spangle Creek Road
Valleyford, WA 99036

Re: K072741
Trade Name: Pre~Va Vaginal Lubricant
Dated: March 18, 2008
Received: March 20, 2008

Dear Dr. Clifton,

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require:

Biocompatibility

1. To support the biocompatibility of Pre~Va Vaginal Lubricant, (b)(4) (b)(4) (b)(4) The following testing was conducted (b)(4) : rabbit vaginal irritation, rabbit penile irritation, human skin sensitization, and slug mucosal irritation. The (b)(4) lubricant did not induce any irritation or sensitization reactions in the animals or human subjects. (b)(4) (b)(4) the results of biocompatibility testing provided for the (b)(4) are acceptable for the Pre~Va lubricant.

   However, you have not provided the results of systemic toxicity testing (b)(4) (b)(4) . This information is necessary to assess if repeated use of this product may cause absorption into the vaginal mucosal tissue and possibly cause systemic effects. Please provide the complete protocol and results of systemic toxicity testing for review.

   If you believe that systemic toxicity testing is not necessary for clearance of this lubricant, please provide justification for your decision.

2. In response to Question 5 of our AI letter dated December 21, 2007, regarding the biocompatibility of the applicator to be marketed with Pre~Va lubricant, you provided the

following information:

a) Technical Data Sheets on (b)(4)
b) Drug Master File Access Letter for (b)(4)
c) Statement of Compliance to California's Proposition 65
d) Compliance to CONEG Model Legislation
e) (b)(4) Assay for cytotoxicity

This information is not sufficient to establish the biocompatibility of the applicator for its use with Pre~Va lubricant. Although Item E demonstrates the non-cytotoxic effect of the applicator, Items A-D, while helpful in establishing the safety of the applicator in general, do not specifically address its sensitization or irritation potential. Therefore, additional biocompatibility testing should be conducted to address these issues.

As previously stated in our AI letter, we expect that biocompatibility testing will be conducted on the final version of the applicator after exposure to Pre~Va lubricant in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, in addition to the cytotoxicity testing already provided, sensitization and irritation tests should also be conducted. Per ISO 10993, sensitization testing should include either maximization or mouse local lymph node assay tests, and vaginal irritation testing should be completed to assess irritation. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

In lieu of testing, you may also consider contacting the applicator vendor and/or the applicator resin vendor to investigate if the applicator material is used to manufacture other products with a similar type and duration of patient contact. You will need to provide evidence that the material used for these other products is identical to that used for the proposed applicator and has a history of safe use.

Indications for Use

3. Please note that if you do not provide sufficient testing or justification to the biocompatibility issues raised, you will be asked to remove the following statement from the indications for use, "Pre~Va may be deposited intravaginally using the applicator."

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device.

We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k)(21 CFR 807.87(l)); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. Please note our guidance document entitled, "Guidance for Industry and FDA Staff - FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request.

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions concerning the contents of the letter, please contact Sharon Andrews at (240) 276-4148. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Colin M. Pollard
Chief, Obstetrics and Gynecology
Devices Branch
Division of Reproductive, Abdominal, and
Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

March 21, 2008

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Product: PRE-VA VAGINAL LUBRICANT

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

February 19, 2008

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Device: PRE-VA VAGINAL LUBRICANT

Extended Until: 20-MAR-2008

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

INGfertility

February 13, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

FDA CDRH DMC

FEB 15 2008

Received

RE: K072741
Pre~Va Vaginal Lubricant – extension request

Dear Sir/Madam:

We are in the process of preparing the response to our original 510(k) submission referenced above. Two of the studies that we initiated to answer the reviewers questions will not be complete until Mid March 2008. Consequently, we are will need a further extension for our response.

The purpose of this letter is to officially request an extension of time to submit the completed information.

Please contact me if you have questions or need further information.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

F

F Received

FEB 15 2008

Received

K17

INGfertility, LLC
17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

January 11, 2008

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Device: PRE-VA VAGINAL LUBRICANT

Extended Until: 20-FEB-2008

Based on your recent request, an extension of time has been granted for you to submit the additional information we requested.

If the additional information (AI) is not received by the "Extended Until" date shown above, your premarket notification will be considered withdrawn (21 CFR 807.87(l)). If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the AI request.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

INGfertility

January 8, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

RE: K072741
Pre~Va Vaginal Lubricant

Dear Sir/Madam:

We have received the initial response and request for additional information for our 510(k) submission referenced above. We appreciate the reviewer's insightful comments and questions.

We are in the process of preparing the information requested. However, with this letter we are officially requesting an extension of time to submit the completed information.

Please contact me if you have questions or need further information.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

K72

INGfertility, LLC
17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

INGfertility, LLC
c/o Dennis Clifton, Pharm.D.
Vice President
17206 South Spangle Creek Road
Valleyford, WA 99036

DEC 2 1 2007

Re: K072741
Trade Name: Pre~Va Vaginal Lubricant
Dated: September 24, 2007
Received: September 27, 2007

Dear Dr. Clifton,

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above. We cannot determine if the device is substantially equivalent to a legally marketed predicate device based solely on the information you provided. To complete the review of your submission, we require:

Bench Testing

1. In this submission, you state that Pre~Va will be supplied with an applicator that may be used to deposit the lubricant intravaginally. However, you have not provided any information to assess the compatibility of the applicator with the lubricant. This information is needed to ascertain if any unfavorable interactions may occur between the applicator and the lubricant that will affect the safety of this device for use by couples who are trying to conceive. Please determine if Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator. Your determination of compatibility should take into account both the duration and the environmental conditions (i.e. temperature) of lubricant exposure to the applicator during both normal and exaggerated use conditions.

   Please note that if you are unable to show that Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator, you will not be able to market the applicator for use with the lubricant.

2. Please also determine if Pre~Va remains compatible with both latex and polyurethane condoms after contact with the applicator.

   Please note that if you are unable to show that Pre~Va is compatible with both latex and

polyurethane condoms after contact with the applicator, you will not be able to market the applicator for use with the lubricant, or you will have to remove the claim of "compatible with latex and polyurethane condoms" from the product labeling.

3. You have qualitatively assessed sperm motility after contact with Pre~Va vaginal lubricant and sperm penetration through Pre~Va via visual observation. However, you have not provided a quantitative assessment of sperm motility, which is necessary to objectively determine the effect of Pre~Va vaginal lubricant on sperm motility and velocity parameters. Please provide the complete test protocols, results, and conclusions from this testing.

   If you believe that quantitative analysis of sperm motility is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient, you will be asked to conduct qualitative sperm analysis.

4. You have not provided the results of cervical mucosal penetration testing for the Pre~Va vaginal lubricant. The results of this testing is necessary to determine that the use of Pre~Va vaginal lubricant has no detrimental effect on sperm penetration into the cervical mucous membrane. This testing may be done as either a post-coital test in human subjects or in an animal cervical mucosal model. If you choose to conduct testing on an animal model, please justify the use of the animal model that you select.

   If you believe that cervical mucosal testing is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient you will be asked to complete cervical mucosal testing.

Biocompatibility

5. You state in your submission that the resin utilized for the applicator is in accordance with 21 CFR 177.1520. This regulation describes "substances for use as basic components of single and repeated use food contact surfaces," and therefore, it does not apply to the applicator as it is intended to be used with the Pre~Va vaginal lubricant.

   As a result, you have not provided sufficient information in this submission regarding the biocompatibility of the applicator. Please provide the complete test protocols, results, and conclusions of this testing.

   We expect that biocompatibility testing will be conducted on the final, sterilized version of the device after exposure to Pre~Va lubricant in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation tests should be conducted. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

If you believe that biocompatibility testing is not necessary for clearance of this device, please provide justification for your decision. Please note that if your justification is not sufficient, you will be asked to conduct biocompatibility testing.

Sterilization/Packaging/Shelf-Life

6. You have not provided any information in this submission regarding the sterilization, packaging, or shelf-life of the applicator. Please provide the following information regarding the applicator.

    a. Describe the method and procedure of sterilization. If the applicator is not provided sterile, justify why sterilization is not necessary for the device as it is intended to be used.
    b. Describe how the applicator will be packaged. If the applicator is provided sterile, describe how the packaging maintains device sterility.
    c. Provide a shelf-life for the applicator, and describe in detail how this shelf-life was determined. The shelf-life of the applicator should meet or exceed the two year shelf life of the lubricant.

Indications for Use

7. Please note that if you do not provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies, you will be asked to remove the following statement(s) from the indications for use, "Pre~Va is safe for use by couples trying to conceive," and/or "Pre~Va may be deposited intravaginally using the applicator."

8. Your indications for use statement contains the following statement, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of a medical device." Please rephrase this statement to read as follows, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions." Your indications for use page and 510(k) summary page should be updated accordingly.

    Please note that as state previously, this change will only be necessary if you provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies.

Labeling

9. The principle display front of the package labeling contains the following statement, "Clinically Tested and Doctor Recommend." However, you have not provided any data in this submission to support this claim. Please provide data to sufficiently justify this claim, or please remove this claim from the labeling.

   In addition, if you sufficiently justify this claim, please rephrase this claim to read as follows, "Clinically Tested and Doctor Recommended."

10. In your submission, the applicator is described as disposable; however, the instructions for use contain do not describe how to dispose of the applicator after use. In order to avoid reuse of the applicator, please add the following statement to the end of the instructions for use on the package labeling, lubricant tube, and the package insert, "The applicator is single use only. Dispose applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."

11. Please place the storage conditions for the Pre~Va vaginal lubricant on the lubricant tube labeling.

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device.

We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at:
http://www.fda.gov/cdrh/modact/leastburdensome.html

You may not market this device until you have provided adequate information described above and required by 21 CFR 807.87(l), and you have received a letter from FDA allowing you to do so. If you market the device without conforming to these requirements, you will be in violation of the Federal Food, Drug, and Cosmetic Act (Act). You may, however, distribute this device for investigational purposes to obtain clinical data if needed to establish substantial equivalence. Clinical investigations of this device must be conducted in accordance with the investigational device exemption (IDE) regulations.

If the information, or a request for an extension of time, is not received within 30 days, we will consider your premarket notification to be withdrawn and your submission will be deleted from our system. If you submit the requested information after 30 days it will be considered and processed as a new 510(k)(21 CFR 807.87(l)); therefore, all information previously submitted must be resubmitted so that your new 510(k) is complete. Please note our guidance document entitled, "Guidance for Industry and FDA Staff - FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Performance Assessment". If the submitter does submit a written request for an extension, FDA will permit the 510(k) to remain on hold for up to a maximum of 180 days from the date of the additional information request.

The purpose of this document is to assist agency staff and the device industry in understanding how various FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act. You may review this document at http://www.fda.gov/cdrh/mdufma/guidance/1219.html.

The requested information, or a request for an extension of time, should reference your above 510(k) number and should be submitted in duplicate to:

Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions concerning the contents of the letter, please contact Sharon Andrews at (240) 276-4148. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

for Colin M. Pollard
Chief, Obstetrics and Gynecology
Devices Branch
Division of Reproductive, Abdominal, and
Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

DEC 2 0 2007

INGfertility, LLC
c/o Dennis Clifton, Pharm.D.
Vice President
17206 South Spangle Creek Road
Valleyford, WA 99036

DEC 2 1 2007

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Dated: September 24, 2007
Received: September 27, 2007

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http://www.fda.gov/cdrh/modact/leastburdensome.html

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Food and Drug Administration
Center for Devices and
Radiological Health
Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions concerning the contents of the letter, please contact Sharon Andrews at (240) 276-4148. If you need information or assistance concerning the IDE regulations, please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or at (240) 276-3150, or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Colin M. Pollard
Chief, Obstetrics and Gynecology
Devices Branch
Division of Reproductive, Abdominal, and
Radiological Devices
Office of Device Evaluation
Center for Devices and Radiological Health

cc: HFZ-401 DMC
HFZ-404 510(k) Staff
HFZ-470 DRARD
D.O.

DRAFT: SMA, 12-18-07
FINAL: clr 12.20.07

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
HFZ-470	S. Andrews	12/20/07						
~~HFZ-470~~		12/20/07						

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-40
9200 Corporate Blvd.
Rockville, Maryland 20850

November 15, 2007

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Received: 14-NOV-2007
Product: PRE-VA VAGINAL LUBRICANT

The Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH), has received the Premarket Notification, (510(k)), you submitted in accordance with Section 510(k) of the Federa Food, Drug, and Cosmetic Act(Act) for the above referenced product and for the above referenced 510(k) submitter. Please note, if the 510(k) submitter is incorrect, please notify the 510(k) Staff immediately. We have assigned your submission a unique 510(k) number that is cited abov Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. We will notify you whe the processing of your 510(k) has been completed or if any additional information is required. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (DMC)(HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official 510(k) submission.

Please note the following documents as they relate to 510(k) review: 1)Guidance for Industry and FDA Staff entitled, "FDA and Industry Actio on Premarket Notification (510(k))Submissions: Effect on FDA Review Clock and Performance Assessment". The purpose of this document is to assist agency staff and the device industry in understanding how variou FDA and industry actions that may be taken on 510(k)s should affect the review clock for purposes of meeting the Medical Device User Fee and Modernization Act (MDUFMA). Please review this document at www.fda.gov/cdrh/mdufma/guidance/1219.html. 2)Guidance for Industry an FDA Staff entitled, "Format for Traditional and Abbreviated 510(k)s". This guidance can be found at www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an origin submission for a Traditional or Abbreviated 510(k). 3)Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review". Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html.

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, HDE) with an electron copy. For more information about the program, including the formatting requirements, please visit our web site at www.fda.gov/cdrh/elecsub.html.

Lastly, you should be familiar with the regulatory requirements for medical devices available at Device Advice www.fda.gov/cdrh/devadvice/" If you have questions on the status of your submission, please contact DSMICA at (240) 276-3150 or the toll-free number (800) 638-2041, or at their Internet address http://www.fda.gov/cdrh/dsma/dsmastaf.html. If you have procedural questions, please contact the 510(k) Staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Office of Device Evaluation
Center for Devices and Radiological Heal

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

September 27, 2007

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Received: 27-SEP-2007
User Fee ID Number: 6032572
Product: PRE-VA VAGINAL LUBRICANT

The Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH), has received the Premarket Notification you submitted in accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act (Act) for the above referenced product. We have assigned your submission a unique 510(k) number that is cited above. Please refer prominently to this 510(k) number in all future correspondence that relates to this submission. YOU MAY NOT PLACE THIS DEVICE INTO COMMERCIAL DISTRIBUTION UNTIL YOU RECEIVE A LETTER FROM FDA ALLOWING YOU TO DO SO.

The Act, as amended by the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) (Public Law 107-250), specifies that a submission shall be considered incomplete and shall not be accepted for filing until fees have been paid (Section 738(f)). Our records indicate that you have not submitted the user fee payment information and therefore your 510(k) cannot be filed and has been placed on hold. Please send a check to one of the addresses listed below:

By Regular Mail	By Private Courier(e.g.,Fed Ex, UPS, etc.)
Food and Drug Administration P.O. Box 956733 St. Louis, MO 63195-6733.	U.S. Bank 956733 1005 Convention Plaza St. Louis, MO 63101 (314) 418-4983

The check should be made out to the Food and Drug Administration referencing the payment identification number, and a copy of the User Fee Cover sheet should be included with the check. A copy of the Medical Device User Fee Cover Sheet should be faxed to CDRH at (240)276-4025 referencing the 510(k) number if you have not already sent it in with your 510(k) submission. After the FDA has been notified of the receipt of your user fee payment, your 510(k) will be filed and the review will begin. If payment has not been received within 30 days, your 510(k) will be deleted from the system. Additional information on user fees and how to submit your user fee payment may be found at www.fda.gov/oc/mdufma.

In all future premarket submissions, we encourage you to provide an electronic copy of your submission. By doing so, you will save FDA resources and may help reviewers navigate through longer documents more easily. Under CDRH's e-Copy Program, you may replace one paper copy of any premarket submission (e.g., 510(k), IDE, PMA, or HDE) with an electronic copy. For more information about the program, including the formatting requirements, please visit our web site at www.fda.gov/cdrh/elecsub.html.

Please note that since your 510(k) has not been reviewed, additional information may be required during the review process and the file may be placed on hold once again. If you are unsure as to whether or not you need to file a 510k Submission with FDA or what type of submission to submit, you should first telephone the Division of Small Manufacturers, International and Consumer Assistance (DSMICA), for guidance at (240) 276-3150 or its toll-fee number (800)638-2041, or contact them at their Internet address www.fda.gov/cdrh/dsma/dsmastaf.html, or you may submit a 513(g) request for information regarding classification to the Document Mail Center at the address above. If you have any questions concerning receipt of your payment, please contact Christina Zeender at Christina.Zeender@fda.hhs.gov. If you have questions regarding the status of your 510(k) Submission, please contact DSMICA at the numbers or address above.

Sincerely yours,

Marjorie Shulman
Consumer Safety Officer
Office of Device Evaluation
Center for Devices and
Radiological Health

K072741

Form Approved: OMB No. 0910-511 Expiration Date: January 31, 2010. See Instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION **MEDICAL DEVICE USER FEE COVER SHEET**	PAYMENT IDENTIFICATION NUMBER: **MD6032572-956733** Write the Payment Identification number on your check.

A completed Cover Sheet must accompany each original application or supplement subject to fees. The following actions must be taken to properly submit your application and fee payment:

1. Electronically submits the completed Cover Sheet to the Food and Drug Administration (FDA) before payment is sent.
2. Include printed copy of this completed Cover Sheet with a check made payable to the Food and Drug Administration. Remember that the Payment Identification Number must be written on the check.
3. Mail Check and Cover Sheet to the US Bank Lock Box, FDA Account, P.O. Box 956733, St. Louis, MO 63195-6733. (*Note: In no case should payment be submitted with the application.*)
4. If you prefer to send a check by a courier, the courier may deliver the check and Cover Sheet to: US Bank, Attn: Government Lockbox 956733, 1005 Convention Plaza, St. Louis, MO 63101. (Note: This address is for courier delivery only. Contact the US Bank at 314-418-4821 if you have any questions concerning courier delivery.)
5. For Wire Transfer Payment Procedures, please refer to the MDUFMA Fee Payment Instructions at the following URL: http://www.fda.gov/cdrh/mdufma/faqs.html#3a. You are responsible for paying all fees associated with wire transfer.
6. Include a copy of the complete Cover Sheet in volume one of the application when submitting to the FDA at either the CBER or CDRH Document Mail Center.

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)	2. CONTACT NAME
BIO ORIGYN LLC 17206 S. Spangle Creek Rd Valleyford WA 99036 US	Dennis Clifton 2.1 E-MAIL ADDRESS dclifton@ingfertility.com 2.2 TELEPHONE NUMBER (include Area code) 509-443-0149 2.3 FACSIMILE (FAX) NUMBER (Include Area code) 509-448-0601
1.1 EMPLOYER IDENTIFICATION NUMBER (EIN) 912111710	

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/dc/mdufma

Select an application type:	3.1 Select one of the types below
[X] Premarket notification(510(k)); except for third party	[X] Original Application
[ ] Biologics License Application (BLA)	Supplement Types:
[ ] Premarket Approval Application (PMA)	[ ] Efficacy (BLA)
[ ] Modular PMA	[ ] Panel Track (PMA, PMR, PDP)
[ ] Product Development Protocol (PDP)	[ ] Real-Time (PMA, PMR, PDP)
[ ] Premarket Report (PMR)	[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)

[X] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA

NO, I am not a small business

4.1 If Yes, please enter your Small Business Decision Number: SBD078100

5. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.

[ ] This application is the first PMA submitted by a qualified small business, including any affiliates, parents, and partner firms

[ ] This biologics application is submitted under secion 351 of the Public Health Service Act for a product licensed for further manufacturing use only

[ ] The sole purpose of the application is to support conditions of use for a pediatric population

[ ] The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

6. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).)

[ ] YES [X] NO

OB II

7. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

$3,326.00 24-Sep-2007

Form FDA 3601 (01/2007)

"Close Window" Print Cover sheet

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

Form Approval
OMB No. 9010-0120
Expiration Date: May 31, 2007.
See OMB Statement on page 5.

Date of Submission	User Fee Payment ID Number	FDA Submission Document Number *(if known)*
01/15/2007	MD6032572-956733	

SECTION A TYPE OF SUBMISSION

PMA	PMA & HDE Supplement	PDP	510(k)	Meeting
☐ Original Submission	☐ Regular (120 day)	☐ Original PDP	☑ Original Submission:	☐ Pre-510(K) Meeting
☐ Premarket Report	☐ Special	☐ Notice of Completion	☑ Traditional	☐ Pre-IDE Meeting
☐ Modular Submission	☐ Panel Track (PMA Only)	☐ Amendment to PDP	☐ Special	☐ Pre-PMA Meeting
☐ Amendment	☐ 30-day Supplement		☐ Abbreviated (Complete section I, Page 5)	☐ Pre-PDP Meeting
☐ Report	☐ 30-day Notice		☐ Additional Information	☐ Day 100 Meeting
☐ Report Amendment	☐ 135-day Supplement		☐ Third Party	☐ Agreement Meeting
☐ Licensing Agreement	☐ Real-time Review			☐ Determination Meeting
	☐ Amendment to PMA & HDE Supplement			☐ Other *(specify):*
	☐ Other			

IDE	Humanitarian Device Exemption (HDE)	Class II Exemption Petition	Evaluation of Automatic Class III Designation (De Novo)	Other Submission
☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ Original Submission	☐ 513(g)
Amendment	Amendment	☐ Additional Information	☐ Additional Information	☐ Other
Supplement	Supplement			*(describe submission):*
	Report			
	Report Amendment			

Have you used or cited Standards in your submission? ☐ Yes ☑ No *(If Yes, please complete Section I, Page 5)*

SECTION B SUBMITTER, APPLICANT OR SPONSOR

Company / Institution Name	Establishment Registration Number *(if known)*		
INGfertility, LLC (Subsidiary of Bio-Origyn, LLC)	3006029862		
Division Name *(if applicable)*	Phone Number *(including area code)*		
	(509) 443-0149		
Street Address	FAX Number *(including area code)*		
17206 S. Spangle Creek Rd	(509) 471-9638		
City	State / Province	ZIP/Postal Code	Country
Valleyford	WA	99036	US
Contact Name			
Dennis Clifton			
Contact Title	Contact E-mail Address		
Vice President	dclifton@ingfertility.com		

SECTION C APPLICATION CORRESPONDENT (e.g., consultant, if different from above)

Company / Institution Name			
Division Name *(if applicable)*	Phone Number *(including area code)*		
	( )		
Street Address	FAX Number *(including area code)*		
	( )		
City	State / Province	ZIP/Postal Code	Country
Contact Name			
Contact Title	Contact E-mail Address		

SECTION D1 REASON FOR APPLICATION - PMA, PDP, OR HDE

- ☐ Withdrawal
- ☐ Additional or Expanded Indications
- ☐ Request for Extension
- ☐ Post-approval Study Protocol
- ☐ Request for Applicant Hold
- ☐ Request for Removal of Applicant Hold
- ☐ Request to Remove or Add Manufacturing Site

- ☐ Process change:
  - Manufacturing
  - Sterilization
  - Packaging
  - Other *(specify below)*

- ☐ Response to FDA correspondence:

- ☐ Change in design, component, or specification:
  - Software / Hardware
  - Color Additive
  - Material
  - Specifications
  - Other *(specify below)*

- ☐ Labeling change:
  - Indications
  - Instructions
  - Performance
  - Shelf Life
  - Trade Name
  - Other *(specify below)*

- ☐ Location change:
  - Manufacturer
  - Sterilizer
  - Packager

- ☐ Report Submission:
  - Annual or Periodic
  - Post-approval Study
  - Adverse Reaction
  - Device Defect
  - Amendment

- ☐ Change in Ownership
- ☐ Change in Correspondent
- ☐ Change of Applicant Address

- ☐ Other Reason *(specify):*

SECTION D2 REASON FOR APPLICATION - IDE

- ☐ New Device
- ☐ New Indication
- ☐ Addition of Institution
- ☐ Expansion / Extension of Study
- ☐ IRB Certification
- ☐ Termination of Study
- ☐ Withdrawal of Application
- ☐ Unanticipated Adverse Effect
- ☐ Notification of Emergency Use
- ☐ Compassionate Use Request
- ☐ Treatment IDE
- ☐ Continued Access

- ☐ Change in:
  - Correspondent / Applicant
  - Design / Device
  - Informed Consent
  - Manufacturer
  - Manufacturing Process
  - Protocol - Feasibility
  - Protocol - Other
  - Sponsor

- ☐ Report submission:
  - Current Investigator
  - Annual Progress Report
  - Site Waiver Report
  - Final

- ☐ Repose to FDA Letter Concerning:
  - Conditional Approval
  - Deemed Approved
  - Deficient Final Report
  - Deficient Progress Report
  - Deficient Investigator Report
  - Disapproval
  - Request Extension of Time to Respond to FDA
  - Request Meeting
  - Request Hearing

- ☐ Other Reason *(specify):*

SECTION D3 REASON FOR SUBMISSION - 510(k)

- ☑ New Device
- ☐ Additional or Expanded Indications
- ☐ Change in Technology

- ☐ Other Reason *(specify):*

SECTION E ADDITIONAL INFORMATION ON 510(K) SUBMISSIONS

Product codes of devices to which substantial equivalence is claimed

1	NUC	2		3		4	
5		6		7		8	

Summary of, or statement concerning, safety and effectiveness information

- [x] 510 (k) summary attached
- [ ] 510 (k) statement

Information on devices to which substantial equivalence is claimed *(if known)*

	510(k) Number		*Trade or Proprietary or Model Name*		*Manufacturer*
1	K051436	1	Pre` Vaginal Lubricant	1	INGfertility
2		2		2	
3		3		3	
4		4		4	
5		5		5	
6		6		6	

SECTION F PRODUCT INFORMATION - APPLICATION TO ALL APPLICATIONS

Common or usual name or classification

lubricant, patient, vaginal, latex compatible

	Trade or Proprietary or Model Name for This Device		Model Number
1	Pre~Va Vaginal Lubricant	1	
2		2	
3		3	
4		4	
5		5	

FDA document numbers of all prior related submissions *(regardless of outcome)*

1	2	3	4	5	6
7	8	9	10	11	12

Data Included in Submission

- [x] Laboratory Testing
- [ ] Animal Trials
- [ ] Human Trials

SECTION G PRODUCT CLASSIFICATION - APPLICATION TO ALL APPLICATIONS

Product Code	C.F.R. Section *(if applicable)*	Device Class
NUC	21 CFR 884.5300	[ ] Class I [x] Class II
Classification Panel		[ ] Class III [ ] Unclassified
lubricant, patient, vaginal, latex compatible		

Indications *(from labeling)*

• To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to insertion of a medical device.
• As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms

Note: Submission of this information does not affect the need to submit a 2891 or 2891a Device Establishment Registration form.	FDA Document Number *(if known)*

SECTION H MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

☑ Original ☐ Add ☐ Delete	FDA Establishment Registration Number (b)(4)	☑ Manufacturer ☐ Contract Sterilizer ☑ Contract Manufacturer ☑ Repackager / Relabeler	
Company / Institution Name (b)(4)		Establishment Registration Number (b)(4)	
Division Name *(if applicable)*		Phone Number *(including area code)* ((b)(4)	
Street Address (b)(4)		FAX Number *(including area code)* (b)(4)	
City (b)(4)	State / Province (b)	ZIP/Postal Code (b)(4)	Country USA
Contact Name (b)(4)	Contact Title Project Manager	Contact E-mail Address (b)(4)	

☐ Original ☐ Add ☐ Delete	FDA Establishment Registration Number	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler	
Company / Institution Name		Establishment Registration Number	
Division Name *(if applicable)*		Phone Number *(including area code)* ( )	
Street Address		FAX Number *(including area code)* ( )	
City	State / Province	ZIP/Postal Code	Country
Contact Name	Contact Title	Contact E-mail Address	

☐ Original ☐ Add ☐ Delete	FDA Establishment Registration Number	☐ Manufacturer ☐ Contract Sterilizer ☐ Contract Manufacturer ☐ Repackager / Relabeler	
Company / Institution Name		Establishment Registration Number	
Division Name *(if applicable)*		Phone Number *(including area code)* ( )	
Street Address		FAX Number *(including area code)* ( )	
City	State / Province	ZIP/Postal Code	Country
Contact Name	Contact Title	Contact E-mail Address	

SECTION I	UTILIZATION OF STANDARDS				
Note: Complete this section if your application or submission cites standards or includes a *"Declaration of Conformity to a Recognized Standard"* statement.					
1	Standards No.	Standards Organization	Standards Title	Version	Date
2	Standards No.	Standards Organization	Standards Title	Version	Date
3	Standards No.	Standards Organization	Standards Title	Version	Date
4	Standards No.	Standards Organization	Standards Title	Version	Date
5	Standards No.	Standards Organization	Standards Title	Version	Date
6	Standards No.	Standards Organization	Standards Title	Version	Date
7	Standards No.	Standards Organization	Standards Title	Version	Date

Please include any additional standards to be cited on a separate page.

Public reporting burden for this collection of information is estimated to average 0.5 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Food and Drug Administration
CDRH (HFZ-342)
9200 Corporate Blvd.
Rockville, MD 20850

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control

INGfertility

September 24, 2007

Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

Dear Sir/Madam:

Enclosed please find two copies of an original Traditional 510(k) application from INGfertility, LLC (subsidiary of Bio-Origyn, LLC). This application is for a new Class II device under Product Code NUC (Lubricant, Vaginal, Patient, Condom Compatible). The proprietary name of the product is *Pre~Va Vaginal Lubricant.*

The predicate for this device is Pre' Vaginal Lubricant (510(k) number K051436) which was previously submitted by INGfertility. To assist in the review, we have also included a complete copy of the Pre' Vaginal Lubricant 510(k) submission documents (inclusive of reviewer's comments).

Information provided in this application demonstrates that the new device is substantially equivalent to its predicate and that the device is effective and safe for its intended use.

Please contact me if you have questions or need further information.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

Table of Contents
Pre~Va Vaginal Lubricant

18	**Software**	N/A
19	**Electomagnetic Compatibility & Electrical Safety**	N/A
20	**Peformance Testing – Bench**	N/A
21	**Performance Testing – Animal**	N/A
22	**Performance Testing - Clinical**	N/A
23	**Appendices**	
Appendix A.	Examples of Applicators for use with Pre~Va	
Appendix B	Validated Instructions for Steam Sterilization	
Appendix C	Certificate of Analysis Template	

SCREENING CHECKLIST FOR ALL PREMARKET NOTIFICATION [510(k)] SUBMISSIONS

510(k) Number: _____

The cover letter clearly identifies the type of 510(k) submission as **(Check the appropriate box)**:

☒ Special 510(k) - Do Sections 1 and 2

☒ Abbreviated 510(k) - Do Sections 1, 3 and 4

X Traditional 510(k) or no identification provided - Do Sections 1 and 4

Section 1: Required Elements for All Types of 510(k) submissions:

	Present or Adequate	Missing or Inadequate
Cover letter, containing the elements listed on page 3-2 of the Premarket Notification [510)] Manual.	✓	
Table of Contents.	✓	
Truthful and Accurate Statement.	✓	
Device's Trade Name, Device's Classification Name and Establishment Registration Number.	✓	
Device Classification Regulation Number and Regulatory Status (Class I, Class II, Class III or Unclassified).	✓	
Proposed Labeling including the material listed on page 3-4 of the Premarket Notification [510)] Manual.	✓	
Statement of Indications for Use that is on a separate page in the premarket submission.	✓	
Substantial Equivalence Comparison, including comparisons of the new device with the predicate in areas that are listed on page 3-4 of the Premarket Notification [510)] Manual.	✓	
510(k) Summary or 510(k) Statement.	✓	
Description of the device (or modification of the device) including diagrams, engineering drawings, photographs or service manuals.	✓	

Identification of legally marketed predicate device. *	✓	
Compliance with performance standards. * [See Section 514 of the Act and 21 CFR 807.87 (d).]	N/A	
Class III Certification and Summary. **	N/A	
Financial Certification or Disclosure Statement for 510(k) notifications with a clinical study. * [See 21 CFR 807.87 (i)]	N/A	
510(k) Kit Certification ***	N/A	

* - May not be applicable for Special 510(k)s.
** - Required for Class III devices, only.
*** - See pages 3-12 and 3-13 in the Premarket Notification [510)] Manual and the Convenience Kits Interim Regulatory Guidance.

Section 2: Required Elements for a SPECIAL 510(k) submission:

	Present	Inadequate or Missing
Name and 510(k) number of the submitter's own, unmodified predicate device.		
A description of the modified device and a comparison to the sponsor's predicate device.		
A statement that the intended use(s) and indications of the modified device, as described in its labeling are the same as the intended uses and indications for the submitter's unmodified predicate device.		
Reviewer's confirmation that the modification has not altered the fundamental scientific technology of the submitter's predicate device.		
A Design Control Activities Summary that includes the following elements (a-c):		
a. Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.		
b. Based on the Risk Analysis, an identification of the required verification and validation activities, including the methods or tests used and the acceptance criteria to be applied.		
c. A Declaration of Conformity with design controls that includes the following statements:		

A statement that, as required by the risk analysis, all verification and validation activities were performed by the designated individual(s) and the results of the activities demonstrated that the predetermined acceptance criteria were met. This statement is signed by the individual responsible for those particular activities.		
A statement that the manufacturing facility is in conformance with the design control procedure requirements as specified in 21 CFR 820.30 and the records are available for review. This statement is signed by the individual responsible for those particular activities.		

Section 3: Required Elements for an ABBREVIATED 510(k)* submission:

	Present	**Inadequate or Missing**
For a submission, which relies on a guidance document and/or special control(s), a summary report that describes how the guidance and/or special control(s) was used to address the risks associated with the particular device type. (If a manufacturer elects to use an alternate approach to address a particular risk, sufficient detail should be provided to justify that approach.)		
For a submission, which relies on a recognized standard, a declaration of conformity [For a listing of the required elements of a declaration of conformity, **SEE Required Elements for a Declaration of Conformity to a Recognized Standard,** which is posted with the 510(k) boilers on the **H drive.]**		
For a submission, which relies on a recognized standard without a declaration of conformity, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device.		
For a submission, which relies on a non-recognized standard that has <u>not</u> been historically accepted by FDA, a statement that the manufacturer intends to conform to a recognized standard and that supporting data will be available before marketing the device <u>and</u> any additional information requested by the reviewer in order to determine substantial equivalence.		

Any additional information, which is not covered by the guidance document, special control, recognized standard and/or non-recognized standard, in order to determine substantial equivalence.		

* - When completing the review of an abbreviated 510(k), please fill out an Abbreviated Standards Data Form (located on the H drive) and list all the guidance documents, special controls, recognized standards and/or non-recognized standards, which were noted by the sponsor.

Section 4: Additional Requirements for ABBREVIATED and TRADITIONAL 510(k) submissions (If Applicable):

	Present	Inadequate or Missing
a) Biocompatibility data for all patient-contacting materials, OR certification of identical material/formulation:	✓	
b) Sterilization and expiration dating information:	✓	
i) sterilization process	✓	
ii) validation method of sterilization process	✓	
iii) SAL	✓	
iv) packaging	N/A	
v) specify pyrogen free	N/A	
vi) ETO residues	✓	
vii) radiation dose	✓	
viii) Traditional Method or Non-Traditional Method	✓	
c) Software Documentation:	N/A	

Items with checks in the "Present or Adequate" column do not require e additional information from the sponsor. Items with checks in the " Missing or Inadequate" column must be submitted before substantive review of the document.

Passed Screening _____Yes _____No
Reviewer:_____
Concurrence by Review Branch:_____

Date:_____

The deficiencies identified above represent the issues that we believe need to be resolved before our review of your 510(k) submission can be successfully completed. In developing the deficiencies, we carefully considered the statutory criteria as defined in

Section 513(i) of the Federal Food, Drug, and Cosmetic Act for determining substantial equivalence of your device. We also considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

Uploaded on March 3, 2004

Indications for Use

510(k) Number (if known): _____

Device Name: Pre~Va Vaginal Lubricant

Indications for Use:

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to insertion of a medical device.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms

Prescription Use _____ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use __X_____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Page __ of ___

510(k) Summary
Pre~Va Vaginal Lubricant

I. General Information on Submitter

Address:	INGfertility, LLC (Subsidiary of Bio-Origyn, LLC) 17206 S. Spangle Creek Rd. Valleyford, WA 99036 USA
Telephone:	509.443.0149
Fax:	509.471.9638
Email:	dclifton@ingfertility.com
Contact Person:	G. Dennis Clifton, Pharm.D.
Date Prepared:	May 1, 2007

II. General Information on Device

Proprietary Name:	Pre~Va Vaginal Lubricant
Classification Name:	lubricant, patient, vaginal, latex compatible (21 CFR 884.5300, Product Code NUC)

III. Predicate Devices

Predicate Device	510(k) control #
Pre' Vaginal Lubricant	K051436

IV. Description of Device

This product is a non-sterile, water-based personal lubricant formulated to supplement the body's own natural lubricating fluids. Pre~Va is used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. It is also used as a personal lubricant to supplement the body's own natural lubricating fluids and to enhance the comfort of intimate sexual activity. The formulation does not harm sperm function and has a pH and osmolarity that are physiologic ("balanced") to that of fertile cervical mucus and semen. The product is compatible with latex and polyurethane condoms. Following is the ingredient list for Pre~Va Vaginal Lubricant:

Ingredients
Water
Hydroxyethylcellulose, NF
Pluronic 127, NF
Sodium Chloride, USP
Arabinogalactan
Sodium Phosphate
Carbopol 934P, NF
Methyl Paraben, USP
Sodium Hydroxide, NF
Potassium Phosphate

V. Intended Use

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to insertion of the medical device.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

VI. Technological Characteristics of Device Compared to Predicate Device

All of the technological characteristics of Pre~Va are identical to the predicate device.

VII. Summary of Performance Data

The performance data of Pre~Va are identical to the predicate.

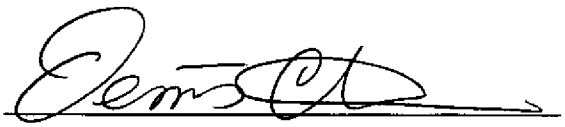
VIII. Conclusion

Pre~Va Vaginal Lubricant is safe for its intended use and substantially equivalent to the predicate device Pre' Vaginal Lubricant.

PREMARKET NOTIFICATION
TRUTHFUL AND ACCURATE STATEMENT

[As Required by 21 CFR 807.87(k)]

I certify that, in my capacity as Vice President of INGfertility, LLC, I believe to the best of my knowledge, that all data and information submitted in the premarket notification are truthful and accurate and that no material fact has been omitted.



G. Dennis Clifton, Pharm.D.

9/24/07

(Date)

_____

Premarket Notification [510(k)] Number

Executive Summary
Pre~Va Vaginal Lubricant

A. Indications For Use

Pre~Va has the following intended uses:

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to insertion of the medical device.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms

B. Principles Of Operation

Pre~Va is a water-based patient lubricant formulated to have a pH and osmolarity, that are physiologic (or balanced) to that of semen and fertile cervical mucus. These properties result in a friction-relieving product that is not harmful to gametes and embryos and thus may be used safely during fertility interventions and during intercourse involving couples trying to conceive.

In order to facilitate device insertion Pre~Va may be applied directly to the instrument prior to use. Alternatively, device insertion may be facilitated by depositing the lubricant intravaginally using the plastic applicator, prior to insertion of the medical device.

C. Composition

Pre~Va is a non-sterile, water-based personal lubricant. (b)(4) (b)(4) (b)(4)

The composition of the applicators used to deposit Pre~Va intravaginally is (b)(4) (b)(4) .The resin utilized for the applicators meets FDA requirements 21CFR 177.1520.

D. Physical Specifications

The following specifications will be utilized to release each lot of Pre~Va Vaginal Lubricant. **These specifications are identical to those used for the predicate.**

Physical Specification/Tests	Ranges/Specifications
pH @ 25°C	7.20 to 7.45
Osmolarity	260 and 360 mOsmo/kg
Apparent Viscosity	8500 to 12,000 cps
Specific Gravity	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens < 100 cfu/ml other organisms
Endotoxin by LAL methodology	< 0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA to > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility following 30-minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium.

E. Safety of Components in Pre~Va

All components of Pre~Va appear either in the FDA Inactive Ingredients List; in the Handbook of Pharmaceutical Excipients as an allowable excipient; in the Cosmetic Ingredient Review as a "monographed" substance; in the Code of Federal Regulations (CFR) as drug or food substance; or are listed as Generally Recognized as Safe (GRAS). Arabinogalactan is also a component (27.5%) of an FDA registered Sperm Processing Medium Device (Isocare One-Step Sperm Processing Media, K023222).

F. Differences Between Pre~Va and Predicate Device

Table 1 provides a detailed comparison of Pre~Va Vaginal Lubricant with its predicate, Pre' Vaginal Lubricant.

As indicated in the table, there are two differences between the Pre~Va and its predicate:

- Pre~Va may be applied intravaginally using a plastic applicator.
- Pre~Va includes in the Intended Use Statement that it is "safe for use by couples trying to conceive" (See Intended Use Statement in Table 1 below).

Neither of these differences raises new questions about efficacy and safety compared to the predicate. The predicate, while not marketed with an

intravaginal applicator, is intended for contact with intravaginal tissues when used for its approved indications. The applicators to be utilized are (b)(4) applicators comprised of (b)(4). The resin utilized for the applicators meets FDA requirements 21CFR 177.1520.

The predicate was cleared for use in fertility interventions, which would include such procedures as embryo transfer, transvaginal collection of oocytes, and Intrauterine insemination. Additionally, the predicate carries a statement on its label urging consumers to "Consult your physician if you have not become pregnant following 6-months use of this product."

Overall, the comparison of intended use and technological characteristics demonstrates the substantial equivalence of the lubricant to the predicate device.

Table 1 Comparison of Features Between New Device And Predicate Device.

Product Name	**Pre~Va Vaginal Lubricant**	**Predicate: Pre' Vaginal Lubricant**
510(k) Control #		K051436
FDA Product Code	NUC	NUC
Intended Use ***[Differences in Italics]***	Pre~Va has the following intended uses: -To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. *Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator prior to insertion of the device.* -As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. *Pre~Va is safe for use by couples trying to conceive* and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.	Pre' has the following intended uses: -To lubricate vaginal tissues to facilitate entry of a diagnostic or therapeutic devices including fertility interventions. -As a personal lubricant to supplement the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. This lubricant may be safely applied to vaginal or penile tissues for lubrication and moisturization purposes. It is also compatible with latex and polyurethane condoms.
Target Population	Home and Clinic Use	Home and Clinic Use
May be used by individuals trying to conceive	**Yes**	**Yes**

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Product Name	Pre~Va Vaginal Lubricant	Predicate: Pre' Vaginal Lubricant
Marketed with intravaginal plastic applicator	Yes	No
Ingredients	Purified water, Sodium Chloride, Sodium Phosphate, Potassium Phosphate, Methylparaben, Arabinogalactan, Hydroxyethylcellulose Carbopol 934P, Pluronic 127, Sodium Hydroxide	Purified water, Sodium Chloride, Sodium Phosphate, Potassium Phosphate Methylparaben, Arabinogalactan, Hydroxyethylcellulose Carbopol 934P, Pluronic 127, Sodium Hydroxide,
Performance	Consumer-use testing demonstrated that Pre~Va resulted in a high level of satisfaction for its moisturizing properties during intercourse".	Consumer-use testing demonstrated that Pre' resulted in a high level of satisfaction for its moisturizing properties during intercourse".
Condom compatible	Yes	Yes
pH @ 25°C	7.20 to 7.45	7.20 to 7.45
Osmolarity	260 and 360 mOsmo/kg	260 and 360 mOsmo/kg
Apparent Viscosity	8500 to 12,000 cps	8500 to 12,000 cps
Specific Gravity	1.0 – 1.05	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens < 100 cfu/ml other organisms	0 cfu/ml pathogens < 100 cfu/ml other organisms
Endotoxin by LAL methodology	< 0.5 EU/ml	< 0.5 EU/ml
Sterile	No	No
Biocompatibility by MEA	1-Cell MEA to > 80% expanded blastocysts at 96 hours	1-Cell MEA to > 80% expanded blastocysts at 96 hours

Product Name	Pre~Va Vaginal Lubricant	Predicate: Pre' Vaginal Lubricant
Biocompatibility by Sperm Motility	Sperm motility following 30-minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium.	Sperm motility following 30-minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium.
Standard Biocompatibility	▪ Vaginal and penile irritation tests carried out in rabbits did not reveal any inflammatory potential under the conditions specified by the protocol. ▪ Pre' caused no irritation or mucosal membrane damage in the Slug Mucosal Irritation test. This tolerance test is used to evaluate the irritation potency of topical formulations including vaginal gels. ▪ Skin sensitization potential when applied to the skin of normal subjects in accordance with a modified Draize Assay revealed no evidence of irritation or sensitization.	▪ Vaginal and penile irritation tests carried out in rabbits did not reveal any inflammatory potential under the conditions specified by the protocol. ▪ Pre' caused no irritation or mucosal membrane damage in the Slug Mucosal Irritation test. This tolerance test is used to evaluate the irritation potency of topical formulations including vaginal gels. ▪ Skin sensitization potential when applied to the skin of normal subjects in accordance with a modified Draize Assay revealed no evidence of irritation or sensitization.

Device Description
Pre~Va Vaginal Lubricant

I. NARRATIVE DESCRIPTION

A. Indications For Use

Pre~Va has the following intended uses:

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to insertion of the medical device.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

B. Principles Of Operation

Pre~Va is a water-based patient lubricant formulated to have a pH and osmolarity that are physiologic or "balanced" to that of semen and fertile cervical mucus. These properties result in a friction-relieving product that is not harmful to gametes and embryos and thus may be used safely during fertility interventions and during intercourse involving couples trying to conceive.

In order to facilitate device insertion Pre~Va may be applied directly to the instrument prior to use. Alternatively, device insertion may be facilitated by depositing the lubricant intravaginally using the plastic applicator prior to insertion of the medical device.

C. Devices With Which The Accessory Or Component May Be Used

- Pre~Va may be used with devices inserted into the vaginal cavity.
- Pre~Va may by used with latex and polyurethane condoms.

D. Variations of the "new" device which INGfertility intends to market

1. Multi-use tubes of product with plastic intravaginal applicators that are filled to pre-marked dose lines by the end users.

II. COMPLETE FORMULATION DESCRIPTION

Pre~Va is a non-sterile, water-based personal lubricant. (b)(4) (b)(4) (b)(4) Table 2 provides the complete description of Pre~Va Vaginal Lubricant's composition.

The applicators to be utilized are (b)(4) applicators comprised of (b)(4) (b)(4) The resin utilized for the applicator meets FDA requirements 21CFR 177.1520. The applicators are manufactured by (b)(4) (b)(4) (FDA Establishment Registration (b)(4) . Samples of the applicators to be utilized are found in ***Appendix A***.

Table 2. Components of Pre~Va Vaginal Lubricant

Ingredients		CAS Reg #	Function	%(Wt/Wt)
Chemical Name	**Trade Name**			
Water		7732-18-5	Solvent	(b)(4)
2-hydroxyethyl cellulose ether, Hydroxyethyl ether cellulose	(b)(4)	9004-62-0	(b)(4)	
Polyethylene–Polypropylene Glycol	Poloxamer, 407, Pluronic F127	9003-11-6	(b)(4)	
Sodium Chloride, USP		7647-14-5	(b)(4)	
Arabinogalactan/Galactoarabinan		9036-66-2		
Sodium phosphate dibasic heptahydrate		7782-85-6		
Acrylic acid polymer; carboxyvinyl polymer; carboxy polymethylene; polyacrylic acid	Carbopol 934P Carbomer 934P	9003 - 01 - 4	(b)(4)	
Benzoic Acid, 4-hydroxy-, methyl ester/ Methyl Paraben, USP		99-76-3	(b)(4)	
Sodium Hydroxide		1310-73-2	(b)(4)	
Phosphoric acid, (b)(4) potassium salt; Potassium (b)(4) phosphate		(b)(4)	p.H Buffer	

III. PHYSICAL SPECIFICATIONS

The following specifications will be utilized to release each lot of Pre~Va Vaginal Lubricant. **These specifications are identical to those used for the predicate.**

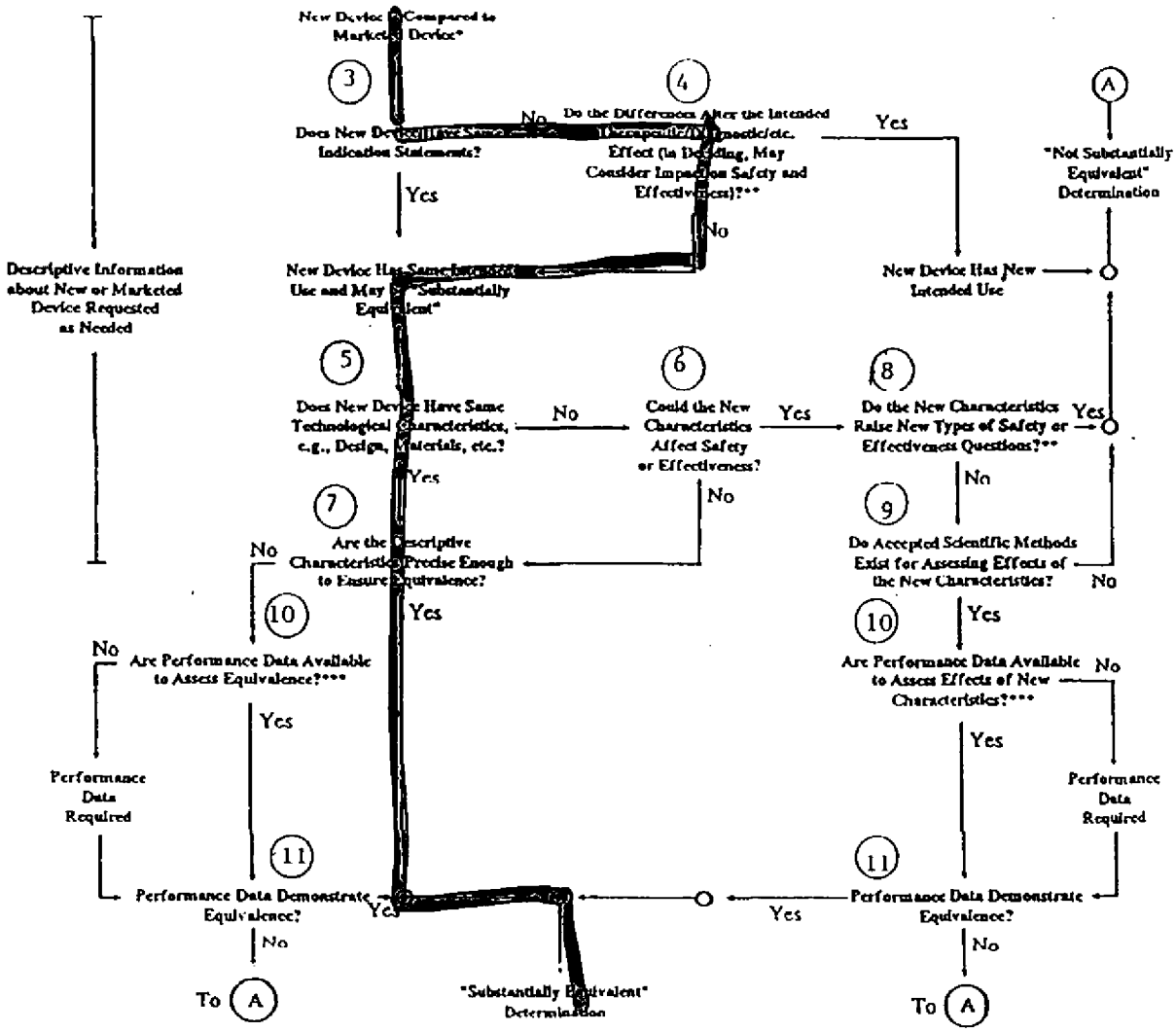
Physical Specification/Tests	Ranges/Specifications
pH @ 25°C	7.20 to 7.45
Osmolarity	260 and 360 mOsmo/kg
Apparent Viscosity	8500 to 12,000 cps
Specific Gravity	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens < 100 cfu/ml other organisms
Endotoxin by LAL methodology	< 0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA to > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility following 30-minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium.

Condom Compatibility
Pre~Va Vaginal Lubricant

(b)(4)

Results from this testing demonstrated that Pre~Va Vaginal Lubricant is compatible with both latex and polyurethane condoms.

510(k) "SUBSTANTIAL EQUIVALENCE" DECISION-MAKING PROCESS (DETAILED)



* 510(k) submissions compare new devices to marketed devices. FDA requests additional information if the relationship between marketed and "predicate" (pre-Amendments or reclassified post-Amendments) devices is unclear.

** This decision is normally based on descriptive information alone, but limited testing information is sometimes required.

*** Data may be in the 510(k), other 510(k)s, the Center's classification files, or the literature.

Substantial Equivalence Discussion
Pre~Va Vaginal Lubricant

Table 3 provides a detailed comparison of Pre~Va Vaginal Lubricant with its predicate Pre' Vaginal Lubricant. This comparison of intended use and technological characteristics demonstrates the substantial equivalence of the lubricant to the predicate device.

I. Differences Between Pre~Va and Predicate Device

A. Intended Use Differences

Two differences exist with regard to the Intended use of Pre~Va compared to the predicate.

1. Pre~Va may be applied intravaginally using a plastic applicator.
2. Pre~Va includes in the Intended Use Statement that it is "…safe for use by couples trying to conceive." (See Intended Use Statement in Table 3 below).

B. Technological Differences

(b)(4) (b)(4) Pre~Va may be deposited intravaginally by use of a piston-type syringe applicator.

II. Intended Use and Technological Differences do not adversely affect Safety and Effectiveness

A. Application Intravaginally

The application of Pre~Va to internal vaginal tissues does not raise new questions about efficacy and safety compared to the predicate. The predicate, while not marketed with an intravaginal applicator, is intended for contact with intravaginal tissues when used for its approved indications.

The applicators to be utilized are (b)(4) applicators comprised of (b)(4 (b)(4)). The resin utilized for the applicator meets FDA requirements 21CFR 177.1520. The applicators are manufactured by (b)(4 (b)(4) Samples of the applicators to be utilized are found in ***Appendix A***.

B. Safe for Couples Trying to Conceive.

Inclusion of the following sentence in the Intended Use Statement does not raise new questions regarding efficacy or safety of the product.

...Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes....

The predicate was cleared for use in fertility interventions, which would include such procedures as embryo transfer, transvaginal collection of oocytes, and Intrauterine insemination. Additionally, the predicate carries the following statement on its approved label (b)(4) **Reviewer's Response):**

Individuals using Pre' while trying to conceive:
• Consult your physician if you have not become pregnant following 6-months use of this product. • No patient data are available regarding viable pregnancies or birth outcomes in patients using this product

Inclusion of the statement that Pre~Va is "safe for use by couples trying to conceive" provides further clarification to the trying-to-conceive consumer that this product can be used if the female experiences a lack of moisture during intercourse while trying to conceive.

Table 3. Comparison of Features Between New Device And Predicate Device.

Product Name	**Pre~Va Vaginal Lubricant**	**Predicate: Pre' Vaginal Lubricant**
510(k) Control #		K051436
FDA Product Code	NUC	NUC
Intended Use ***[Differences in Italics]***	Pre~Va has the following intended uses: -To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. *Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to insertion of the medical device.* -As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. *Pre~Va is safe for use by couples trying to conceive* and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.	Pre' has the following intended uses: -To lubricate vaginal tissues to facilitate entry of a diagnostic or therapeutic devices including fertility interventions. -As a personal lubricant to supplement the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. This lubricant may be safely applied to vaginal or penile tissues for lubrication and moisturization purposes. It is also compatible with latex and polyurethane condoms.
Target Population	Home and Clinic Use	Home and Clinic Use
May be used by individuals trying to conceive	**Yes**	**Yes**

Product Name	Pre~Va Vaginal Lubricant	Predicate: Pre' Vaginal Lubricant
Marketed with intravaginal plastic applicator	Yes	No
Ingredients	Purified water, Sodium Chloride, Sodium Phosphate, Potassium Phosphate [redacted], Methylparaben, Arabinogalactan, Hydroxyethylcellulose [redacted], Carbopol 934P, Pluronic 127, Sodium Hydroxide	Purified water, Sodium Chloride, Sodium Phosphate, Potassium Phosphate [redacted] Methylparaben, Arabinogalactan, Hydroxyethylcellulose [redacted] Carbopol 934P, Pluronic 127, Sodium Hydroxide,
Performance	Consumer-use testing demonstrated that Pre~Va resulted in a high level of satisfaction for its moisturizing properties during intercourse".	Consumer-use testing demonstrated that Pre' resulted in a high level of satisfaction for its moisturizing properties during intercourse".
Condom compatible	Yes	Yes
pH @ 25°C	7.20 to 7.45	7.20 to 7.45
Osmolarity	260 and 360 mOsmo/kg	260 and 360 mOsmo/kg
Apparent Viscosity	8500 to 12,000 cps	8500 to 12,000 cps
Specific Gravity	1.0 – 1.05	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens < 100 cfu/ml other organisms	0 cfu/ml pathogens < 100 cfu/ml other organisms
Endotoxin by LAL methodology	< 0.5 EU/ml	< 0.5 EU/ml
Sterile	No	No
Biocompatibility by MEA	1-Cell MEA to > 80% expanded blastocysts at 96 hours	1-Cell MEA to > 80% expanded blastocysts at 96 hours

Product Name	Pre~Va Vaginal Lubricant	Predicate: Pre' Vaginal Lubricant
Biocompatibility by Sperm Motility	Sperm motility following 30-minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium.	Sperm motility following 30-minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium.
Standard Biocompatibility	▪ Vaginal and penile irritation tests carried out in rabbits did not reveal any inflammatory potential under the conditions specified by the protocol. ▪ Pre' caused no irritation or mucosal membrane damage in the Slug Mucosal Irritation test. This tolerance test is used to evaluate the irritation potency of topical formulations including vaginal gels. ▪ Skin sensitization potential when applied to the skin of normal subjects in accordance with a modified Draize Assay revealed no evidence of irritation or sensitization.	▪ Vaginal and penile irritation tests carried out in rabbits did not reveal any inflammatory potential under the conditions specified by the protocol. ▪ Pre' caused no irritation or mucosal membrane damage in the Slug Mucosal Irritation test. This tolerance test is used to evaluate the irritation potency of topical formulations including vaginal gels. ▪ Skin sensitization potential when applied to the skin of normal subjects in accordance with a modified Draize Assay revealed no evidence of irritation or sensitization.

Proposed Labeling

Pre~Va Vaginal Lubricant

PRINCIPAL DISPLAY FRONT

Logo
Pre~Va ™ Vaginal Lubricant
"Fertility~Friendly*" ™

- pH Balanced to Match Fertile Cervical Mucus
- *Uniquely Developed to Not Harm Sperm
- Applicator Coats Vagina with Moisture
- Compatible with latex and polyurethane condoms

Clinically Tested and Doctor Recommend

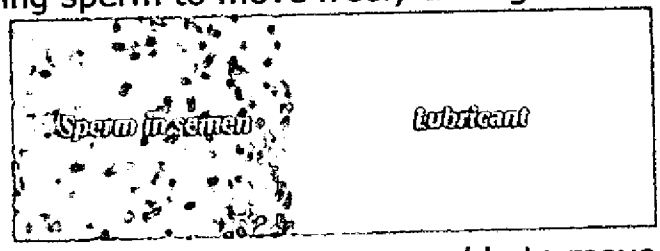
With Arabinoglalactan for Antioxidant Support

40 gm tube with 6 disposable applicators

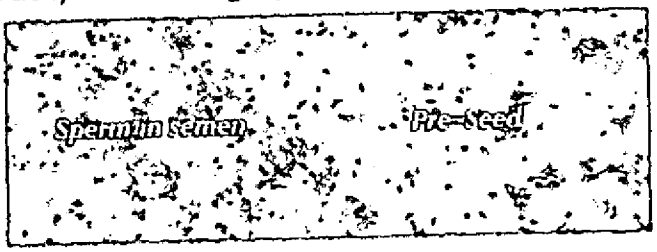
PRINCIPAL DISPLAY PANEL BACK AND SIDES

Pre~Va provides moisture without harming sperm. For use even when trying to conceive- a time of increased vaginal dryness* when most other lubricants should be avoided due to their detrimental effects on sperm**.

Popular lubricants can create a barrier that interferes with the ability of swimming sperm to move freely through them.



In contrast, swimming sperm are able to move freely into Pre~Va.*



*Pictures taken in laboratory at 200X magnification after 10 min of contact between semen and products.

Visit www.pre-va.com to view *clinical studies and published studies**.

DIRECTIONS:
Personal Use:
Pre~Va's moisture can best mimic natural secretions, when applied intravaginally. Remove seal from tube opening before initial use. Remove applicator from pouch and twist firmly onto the tube for filling. Fill applicator with the desired amount of Pre~Va, to relieve vaginal dryness. Insert applicator into vagina to deposit Pre~Va prior to intercourse. See enclosed insert for complete directions and information.

Pre~Va can also be used as an external lubricant. External Lubrication: squeeze a small amount (size of a nickel) onto your fingertips and apply to genital area. Vary amount to achieve desired lubrication. To enhance condom use, add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface.

Clinic Use:
Remove seal from tube opening before initial use.

- Applicator: using aseptic technique, fill applicator with desired amount of lubricant and insert into the vagina prior to insertion of instrument.
- Without Applicator: Using aseptic technique apply desired amount of lubricant to instrument and/or genital area. Vary amount to achieve desired lubrication.

If sterilized product is desired (e.g. intrauterine insemination, embryo transfer) please see package insert for INSTRUCTIONS FOR STERILIZATION.

USES: Pre~Va personal lubricant supplement the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms. Pre~Va is also used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. To facilitate device insertion Pre~Va may be applied directly to the device or may be deposited intravaginally, using an enclosed applicator prior to device insertion.

INGREDIENTS: Purified Water, Hydroxyethylcellulose, Pluronic 127, Sodium Chloride, Sodium Phosphate, Carbopol 934, arabinogalactan, methylparaben, sodium hydroxide, potassium phosphate

Individuals using Pre~Va while trying to conceive:

- Consult your physician if you have not become pregnant following 6-months use of this product.
- No patient data are available regarding viable pregnancies or birth outcomes in patients using this product

Warning: Pre~Va is not a contraceptive. It does not harm sperm or interfere with their function. Keep out of reach of Children.

Caution: If irritation occurs discontinue use immediately, and if it persists consult a physician.

Important: Store at room temperature.

QUESTIONS & INFORMATION: Please call us toll-free at 888.471.7333 or visit us at www.ingfertility.com for detailed product information and to review clinical study data*.

Manufactured in the USA for: INGfertility, Valleyford, WA 99036
US Patent #6,593,309 B2

Expiration Date
Lot #

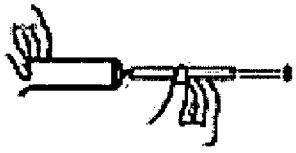
INTERNAL PACKAGE INSERT

USES: Pre~Va personal lubricant supplement the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms. Pre~Va is also used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. To facilitate device insertion Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator.

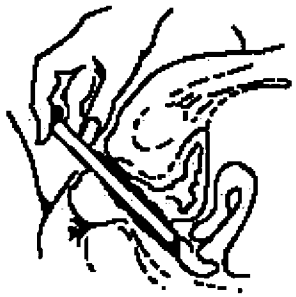
Personal Use

Directions for Using Pre~Va Vaginal Lubricant with Disposable Applicators:

1. Remove seal from tube opening before initial use
2. Pre~Va can be applied up to 15 minutes prior to intercourse. Applying it before you begin making love allow the lubricant to disperse throughout the vagina and allows more spontaneity for you as a couple.
3. Attach the applicator to the tube lubricant by placing twisting the end of the applicator firmly onto tube (see picture).



4. Gently squeeze the lubricant into the applicator, continue squeezing until the applicator is full or the desired amount is present in the applicator. Most women will choose the 3 g fill line to meet their product needs. Separate the applicator from the tube. After each use replace the cap and rollup the tube from the bottom.
5. Gently inset the applicator deep into the vagina. This can be done while standing, lying down or sitting (as if on the toilet).
6. Holding the barrel of the applicator, slowly push the plunger all the way in to release the gel into the vagina (see picture).



7. Remove both parts of the applicator from the vagina.
8. In order to get the right amount of lubricant for your body, bear down slightly after depositing the product. This will expel any excess Pre~Va that your body doesn't need. If desired, then you can then use a tissue to lightly wipe off any product that is on your vulva after application.

Directions for Using Pre~Va Vaginal Lubricant Externally:
Squeeze a small amount (size of a nickel) onto your fingertips and apply to genital area. Vary amount to achieve desired lubrication. To enhance condom use, add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface.

Clinic Use:
Remove seal from tube opening before initial use. If sterilized product is desired (e.g. intrauterine insemination, embryo transfer) please see package insert for INSTRUCTIONS FOR STERILIZATION.

- Applicator: using aseptic technique, fill one of the enclosed applicators
- with desired amount of lubricant and insert into the vagina prior to insertion of instrument.

Without Applicator: Using aseptic technique apply desired amount of lubricant to instrument and/or genital area. Vary amount to achieve desired lubrication.

Individuals using Pre~Va while trying to conceive:

- Consult your physician if you have not become pregnant following 6-months use of this product.
- No patient data are available regarding viable pregnancies or birth outcomes in patients using this product

Warning: Pre~Va is not a contraceptive. It does not harm sperm or interfere with their function. Keep out of reach of Children.

Do not use if quality seal is broken.

Caution: If irritation occurs discontinue use immediately, and if it persists consult a physician.

Important: Store at room temperature.

INGREDIENTS: Purified Water, Hydroxyethylcellulose, Pluronic 127, Sodium Chloride, Sodium Phosphate, Carbopol 934, arabinogalactan, methylparaben, sodium hydroxide, potassium phosphate

QUESTIONS & INFORMATION: Please call us toll-free at 888.471.7333 or visit us at www.ingfertility.com for detailed product information and to review clinical study data*.
Manufactured in the USA for: INGfertility, Valleyford, WA 99036
US Patent #6,593,309 B2

QUALITY ASSURANCE

Each lot of Pre~Va Vaginal Lubricant is tested to ensure the following:

Test	Specification
pH	7.2-7.45
Osmolarity (ion concentration)	260mOsm-360mOsm
Endotoxin by LAL methodology	< 0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility after 30-minute exposure to 10% lubricant solution equal to 80% or more that seen for sperm with no lubricant present.

Results of the mouse embryo assay (MEA), endotoxin testing (LAL), and sperm motility assay are reported on a lot specific Certificate of Analysis, which is available upon request.
Expiration Date
Lot #

VALIDATED INSTRUCTIONS FOR STERILIZATION

1. Moist heat/steam sterilization is the preferred and recommend method for Pre~Va Vaginal Lubricant
2. Using aseptic technique transfer desired quantity of lubricant to a steam-compatible container (e.g. conical centrifuge tube of polypropylene or borosilicate glass). Do not fill the container more than 75% capacity to allow room for expansion. Place the cap on the container but do not tighten. The cap must be loose to ensure proper sterilization and to prevent damage to the container.
3. The recommended steam sterilization parameters are as follows:

Sterilizer Type	Temperature	Full Cycle Time
Gravity	121 °C 250 °F	30 minutes

4. Remove the container from the autoclave. Once the container has cooled tighten the cap.
5. Regularly test the efficacy of steam autoclaves as recommended by the equipment manufacturer or local regulations. Sterilizer manufacturer recommendations for operation and load configuration should be followed explicitly.

Shelf Life
Pre~Va Vaginal Lubricant

(b)(4)

(b)(4)

(b)(4) for the detailed protocol and results for stability testing.

Sterilization
Pre~Va Vaginal Lubricant

I. Summary of Microbial and Sterilization Specifications

Pre~Va Vaginal Lubricant, like its predicate, will be supplied as a non-sterile gel with the following specifications as they relate to microbiology and endotoxin:

Specification	Ranges/Specifications
Microbial limits at 48 hours	0 cfu/ml pathogens < 100 cfu/ml other organisms
Endotoxin by LAL methodology	< 0.5 EU/ml

Validated instructions for sterilization to an SAL (b)(4) have been developed and are included in ***Appendix B.*** These instructions will be provided on the package label for instances when clinics desire sterilized product (e.g. intrauterine insemination, embryo transfer). **These instructions are identical to those used for the predicate.** The instructions can be viewed on page 41 of this application.

(b)(4)

- (b)(4)

II. Certificate of Analysis

A Certificate of Analysis has been developed which will contain lot-specific information on results of sperm motility, MEA, and endotoxin testing of the lubricant, as well as other physical parameters. Please see ***Appendix C*** for the Certificate of Analysis template.

Biocompatibility Assessment
Pre~Va Vaginal Lubricant

I. GENERAL STATEMENT REGARDING DEVICE AND PREDICATE

- (b)(4)
-

II. COMPOSITION OF Pre~Va

The components of Pre~Va are listed below.

Ingredients	Wt/Wt %
Water	(b)(4)
Hydroxyethylcellulose, NF	
Pluronic 127, NF	
Sodium Chloride, USP	
Arabinogalactan	
Sodium Phosphate	
Carbopol 934P, NF	
Methyl Paraben, USP	
Sodium Hydroxide, NF	
Potassium Phosphate	

To support the safety and biocompatibility of Pre~Va an extensive review of each component's previous appearance in drugs, cosmetics, and food are provided. As shown in Table 4, all components of Pre~Va appear either in the FDA Inactive Ingredients List; in the Handbook of Pharmaceutical Excipients; in the Cosmetic Ingredient Review as a "monographed" substance; in the Code of Federal Regulations as drug or food substance; or are listed as Generally Recognized as Safe (GRAS).

Table 4. Existing Listings for Pre~Va Vaginal Lubricant Components

Ingredient	1. FDA Inactive Ingredients List *(for some substances, X is indicated where no level was provided in the inactive ingredient list but the substance appeared in the list.)*	2. Handbook of Pharmaceutical Excipients	3. CIR Compendium or INCI	4. CFR	5. GRAS List
Arabinogalactan or Galactoaribinan**	—	—	Yes	Yes 172.610 (permitted food additives)	Yes
Carbopol 934P	—	Yes	—	701.3 (labeling)	—
Hydroxyethylcellulose	Yes 0.8% topical lotion	Yes	Yes	Yes 349.12 (ophthalmic)	—
Methylparaben	0.2%, vaginal emulsion cream; 0.08%, vaginal gel; X, vaginal suppository; 0.2%, topical ointment ;15%, topical lotion; 62.78%, topical emulsion cream; 70%, topical gel, jelly	Yes	--	Yes 310.545 (drug products)	—
Pluronic 127 (poloxamer 407)	0.16% -0.2% Ophthalmic Solution; 5% Oral Solution; 106.7 Mg Oral Tablet; 1%Topical Emulsion, Cream; 15.5% Topical Gel; X Topical Solution		Yes	—	—

Ingredient (cont.)	1. FDA Inactive Ingredients List	2. Handbook of Pharmaceutical Excipients	3. CIR Compendium or INCI	4. CFR	5. GRAS List
Purified Water	N/A	N/A	N/A	N/A	N/A
Sodium Chloride	0.27% topical solution; 0.5% topical emulsion cream; X topical ointment	Yes	--	--	--
Sodium Hydroxide	0.19% vaginal emulsion cream; 2.6% topical lotion; 10% topical gel; X vaginal gel	--	--	--	--
Sodium Phosphate	0.189% Nasal Solution; 0.81% Ophthalmic Solution; 0.29% Ophthalmic Solution, Drops; 0.2% Ophthalmic Suspension; X Topical Emulsion, Cream; 0.15% Topical Ointment; 0.667%Topical Shampoo; X Topical Shampoo, Suspension	--	--	--	--
Potassium Phosphate (4) (b)	X Intrauterine Solution; 0.14% Nasal Spray; 0.2% Ophthalmic Solution; 0.065% Ophthalmic Solution, Drops; 0.44% Ophthalmic Suspension	--	--	--	--

**Arabinogalactan is also a component (27.5%) of an FDA registered Sperm Processing Medium Device (Isocare One-Step Sperm Processing Media, 510(k) No. K023222).

III. ROUTINE BIOCOMPATIBILITY STUDIES PERFORMED

Appropriate routine biocompatibility studies of Pre~Va have been performed in humans, animals, and invertebrates.

(b)(4)

- Rabbit Vaginal Irritation Studies (b)(4) ***Section 3 Appendix A)***
- Rabbit Penile Irritation Studies (b)(4) ***Section 3 Appendix A)***
- Human Skin Sensitization Studies (b)(4) ***Section 3 Appendix C)***
- Slug Mucosal Irritation Test (b)(4) ***Section 3 Appendix B)***

IV. SPECIAL BIOCOMPATIBILITY STUDIES PERFORMED

Bioactive Effects of Pre~Va on Sperm Function & Embryo Development.

Appropriate assays were performed to demonstrate that Pre~Va does not impair sperm function or embryo development.

(b)(4)

- Effects on fertilization and embryo development
  - Mouse Embryo Assay (b)(4)
    (b)(4)
  - Bovine in vitro fertilization and embryo development
    (b)(4)
- Sperm Motility (b)(4)
  (b)(4)
- Sperm/Lubricant Interactions (b)(4)
  (b)(4)
- Effects on sperm chromatin (b)(4)
  (b)(4)

V. CONCLUSION

Based on the documented presence of Pre~Va components in other drugs, cosmetics, food, and devices, (b)(4)
(b)(4) it is concluded that the device is safe for its intended use.

APPENDIX A
EXAMPLE OF APPLICATOR FOR USE WITH PRE~VA

The applicators to be utilized are (b)(4) comprised (b)(4) (b)(4) The resin utilized for the applicator meets FDA requirements 21CFR 177.1520. The applicators are manufactured (b)(4) (b)(4). An example of the applicators to be utilized is enclosed.

APPENDIX B
VALIDATED INSTRUCTIONS FOR STEAM STERILIZATION

(b)(4),Sterilization Report

(b)(4),Sterilization Report

(b)(4),Sterilization Report

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APPENDIX C
CERTIFICATE OF ANALYSIS
PRE~VA VAGINAL LUBRICANT

INGfertility, LLC
17206 Spangle Creek Road
Valleyford, WA 99036
info@ingfertility.com
p) 509.443.0149
f) 509.448.0601

Certificate of Analysis

Lot Number: _____
Product Description: Pre~Va Vaginal Lubricant
Manufacture Date: ___/__/___
Expiration Date: __/__/____

Test	Result	Specifications
pH		7.2 to 7.45
Osmolality		260 to 360 mOsm/kg
Viscosity		8,500 to 12,000 cps
Microbial Count		
Pathogens		0 CFU/ml
Other Organisms		< 100 CFU/ml
Endotoxin by LAL methodology		< 0.5 EU/ml
Mouse Embryo Assay (MEA): One-Cell MEA exposed to a 5% Pre' solution for 30 minutes.		≥ 80% expanded blastocysts at 96 hours.
Human Sperm Motility following 30-minute exposure to 10% Pre' solution.		Sperm motility equal to 80% or more of control sperm (without lubricant).

_____
Quality Assurance

_____
Date

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Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Sharon Andrews

Subject: 510(k) Number K072741/S2

To: The Record

Please list CTS decision code SE

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_5631/Screening%20Checklist%207%202%2007.doc)

☐ Hold (Additional Information or Telephone Hold).

☑ Final Decision (SE) SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	*Attach IFU*	✓	
510(k) Summary /510(k) Statement	*Attach Summary*	✓	
Truthful and Accurate Statement.	*Must be present for a Final Decision*	✓	
Is the device Class III? If yes, does firm include Class III Summary?	*Must be present for a Final Decision*		✓
Does firm reference standards? (If yes, please attach form from http://www.fda.gov/opacom/morechoices/fdaforms/FDA-3654.pdf)			✓
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC			✓
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			✓
Is this device intended for pediatric use only?			✓
Is this a prescription device? (If both prescription & OTC, check both boxes.)			✓
Is clinical data necessary to support the review of this 510(k)? Did the application include a completed FORM FDA 3674, *Certification with Requirements of ClinicalTrials.gov Data Bank*? (If not, then applicant must be contacted to obtain completed form.)			✓
Does this device include an Animal Tissue Source?			✓
All Pediatric Patients age<=21			
Neonate/Newborn (Birth to 28 days)			
Infant (29 days -< 2 years old)			
Child (2 years -< 12 years old)			
Adolescent (12 years -< 18 years old)			
Transitional Adolescent A (18 - <21 years old) Special considerations are being given to this group, different from adults age ≥ 21 (different device design or testing, different protocol procedures, etc.)			
Transitional Adolescent B (18 -<= 21; No special considerations compared to adults => 21 years old)		✓	
Nanotechnology			✓

Is this device subject to Section 522 Postmarket Surveillance? (Postmarket Surveillance Guidance, http://www.fda.gov/cdrh/osb/guidance/316.html)	*Contact OSB.*		✓
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC.*		✓

Regulation Number	**Class***	**Product Code**
21 CFR 884.5300	II	NUC

(*If unclassified, see 510(k) Staff)

Additional Product Codes: _____

Review: Colin M Pollard (Branch Chief) OGDB (Branch Code) 7/15/08 (Date)

Final Review: _____ (Division Director) 7/16/08 (Date)

DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
Traditional/Abbreviated

K072741/S002

Date: July 15, 2008
To: The Record
From: Sharon Andrews, Biomedical Engineer

Office: ODGB
Division: DRARD

510(k) Holder: INGfertility, LLC
Device Name: Pre~Va Vaginal Lubricant
Contact: Dennis Clifton, Pharm.D., Vice President
Address: 17206 South Spangle Creek Road, Valleyford, WA 99036
Phone: 509-443-0149
Fax: 509-471-9638
Email: dclifton@ingfertility.com

I. Purpose and Submission Summary

The 510(k) holder would like to introduce the Pre~Va Vaginal Lubricant into interstate commerce. Pre~Va is a personal lubricant that is compatible with both latex and polyurethane condoms. It may also be used to lubricate devices used during fertility interventions and is safe for use by couples trying to conceive. Pre~Va will also be marketed with an applicator for intravaginal deposition.

This is the third round of review of this submission. The sponsor was sent letters requesting additional information on December 21, 2007 and April 25, 2008. The sponsor has resolved all the remaining deficiencies. I believe that the Pre~Va Vaginal Lubricant is substantially equivalent to its predicate device.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use page (OTC)	X		
Truthful and Accuracy Statement	X		
510(k) Summary or 510(k) Statement	X		
Standards Form			X

III. Device Description

	Yes	No	N/A
Is the device life-supporting or life sustaining?		X	

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	Yes	No	N/A
Is the device an implant (implanted longer than 30 days)?		X	
Does the device design use software?		X	
Is the device sterile?		X	
Is the device reusable (not reprocessed single use)?		X	
Are "cleaning" instructions included for the end user?			X

Pre~Va Vaginal lubricant is a Class II vaginal latex compatible vaginal patient lubricant classified under 21 CFR 884.5300 and procode NUC.

The formulation of Pre~Va Vaginal lubricant, including the respective weight percent, function, and Chemical Abstracts Service (CAS) Numbers of each ingredient are listed in the table below.

Ingredient	Weight Percent (%w/w)	Function	CAS Number
Water	(b)(4)	Solvent	7732-18-5
Hydroxyethylcellulose, NF		(b)(4)	9004-62-0
Pluronic 127, NF			9003-11-6
Sodium Chloride, USP			7647-14-5
Arabinogalactan			9036-66-2
Sodium Phosphate			(b)(4)
Carbopol 934P, NF			9003-01-4
Methylparaben, USP			99-76-3
Sodium Hydroxide, NF			1310-73-2
Potassium Phosphate			(b)(4)

The specifications of Pre~Va are outlined in the following table.

Physical Specifications/Tests	Ranges/Specifications
pH @ 25°C	7.20 – 7.45
Osmolarity	260 and 360 mOsmo/kg
Apparent Viscosity	8,500 – 12,000 cps
Specific Gravity	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens; <100 cfu/ml other organisms
Endotoxin by LAL methodology	<0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA to > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility following 30 minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium

Pre~Va will be supplied with an applicator. The sponsor provided three samples of the applicator with the

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submission. The applicator has a piston style design and is made of (b)(4) (b)(4). The resin utilized for the applicator is in accordance with 21 CFR 177.1520, which describes "substances for use as basic components of single and repeated use food contact surfaces." This regulation is not applicable to the applicator for use with a lubricant.

The applicators are manufactured by (b)(4). The sponsor has provided engineering drawings noting the dimensions for the applicator. The fully extended length of the applicator is 8.9 inches, and the fully compressed length of the applicator is 4.9 inches. The diameter of the applicator at its widest point is 0.56 inches. The applicator is marked with the following fill lines, 0.5, 1, 2, 3, and 4 grams. The maximum volume the applicator can hold is 5 grams.

The applicator can be screwed onto the lubricant tube, and the lubricant can be squeezed into the applicator to a desired amount. The applicator is disposable.

IV. Indications for Use

Pre~Va vaginal lubricant is intended to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. *Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.* As a personal lubricant, Pre~Va supplements the body's own natural lubrication fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. *Pre~Va is safe for use by couples trying to conceive* and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

V. Predicate Device Comparison

The predicate device for the subject lubricant is the Pre' vaginal lubricant, also marketed by INGFertility. Pre' vaginal lubricant is intended to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. As a personal lubricant, Pre' supplements the body's own natural lubrication fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre' may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

Pre' vaginal lubricant was cleared under 510(k) K051436 on October 13, 2006. It is classified as a condom under 21 CFR 884.5300 and procode NUC.

The intended use of the subject and predicate lubricants is not the same. The subject lubricant has an expanded indication, which is italicized above in Section IV – Indications for Use. However, the difference in the intended use does not alter the intended therapeutic or diagnostic effect.

(b)(4)

There are two primary differences between the predicate and subject lubricants: (1) the subject lubricant claims to safe to use by couples trying to conceive, and (2) the subject lubricant is packaged with a (b)(4) applicator. The consequences of these changes are discussed below in the appropriate sections of this review memo.

VI. Labeling

Labeling has been provided which includes instructions for use and an appropriate prescription statement

as required by CFR 21.807.87 (e). This product will be sold over the counter.

The sponsor has provided draft labeling that will be found on the lubricant package, the lubricant tube, and a draft package insert.

The package labeling contains the following information: product claims, directions for use (personal and clinical), ingredients, warnings, caution statements, storage information, expiration date, and lot number.

The package labeling contains the following information: product claims, directions for use (personal and clinical), ingredients, warnings, caution statements, expiration date, and lot number.
The sponsor will be asked to place the storage information on the lubricant tube labeling.

The package insert contains more detailed instructions for use, warnings, caution statements, storage information, ingredients, products specifications, and validated instructions for sterilization.

The labeling for this product is acceptable.

VII. Sterilization/Shelf Life/Reuse

Pre~Va vaginal lubricant is supplied non-sterile. It is specified to have microbial limits at 48 hours of 0 cfu/ml pathogens and <100 cfu/ml other organisms. The endotoxin limit is <0.5 EU/ml. These are identical to the specifications of the predicate lubricant.

The clinical instructions for use found in the package insert provide instructions for sterilization to a SAL (b)(4) This is for when clinics desire a sterilized product for procedures such as intrauterine insemination and embryo transfer. These instructions are identical to those supplied with the predicate lubricant.

Stability testing was conducted (b)(4)
(b)(4)
Samples were found to be within range for all intervals tested according to the table below.

Physical Specification	Acceptable Range
(b)(4)	(b)(4)

In addition, the following testing was conducted upon completion of stability testing:

a) (b)(4)
b)
c)
d)

The details of this testing are described in Section XI – Performance Testing – Bench. The results of this testing are acceptable.

The stability data collected was used to establish a shelf-life of two years (b)(4)
(b)(4)

The applicator will be provided non-sterile. For more information, please see Addendum – Sponsor Response to December 21, 2007 AI Letter – Question 6.

VIII. Biocompatibility

This lubricant is a surface device that is in contact with both the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation activity tests must be completed.

The following biocompatibility testing was conducted (b)(4) rabbit vaginal irritation, rabbit penile irritation, human skin sensitization, and slug mucosal irritation. (b)(4) lubricant did not induce any irritation or sensitization reactions in the animals or human subjects. (b)(4) (b)(4) the results of biocompatibility testing (b)(4) are acceptable for the Pre~Va lubricant.

(b)(4) systemic toxicity testing (b)(4) This issue was discussed with Dr. Michael Bailey, OGDB Biologist, and Colin Pollard, OGDB Branch Chief. It was decided that the sponsor should be asked to conduct this testing as this is now standard lubricant review policy. Because of the repeated use nature of a lubricant, it is possible that it could be absorbed, and thus result in systemic effects. The sponsor conducted systemic toxicity testing as requested. The results of this testing are acceptable. For more information, please see Section XIV – Sponsor Response to April 25, 2008 AI Letter – Question 1.

The sponsor has also assessed the biocompatibility of the applicator. Based upon the information provided, the applicator is biocompatible. For more information, please see Addendum – Sponsor Response to December 21, 2007 AI Letter – Question 5 and Section XIV – Sponsor Response to April 25, 2008 AI Letter – Question 2.

IX. Software

This section does not apply to this submission.

X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

This section does not apply to this submission.

XI. Performance Testing – Bench

Lubricant/Applicator Compatibility

The sponsor has provided testing assessing the compatibility of the lubricant and the applicator. The results of this testing are acceptable. The details of this testing can be found in Addendum – Sponsor Response to December 21, 2007 AI Letter – Question 1.

(b)(4)

Condom Compatibility

Condom compatibility testing was conducted by (b)(4) Results from this testing indicated the (b)(4) lubricant was compatible with both latex and polyurethane condoms and that the use of the lubricant had no statistically significant effects on tensile strength, elongation at break, or breaking force. Burst testing was not conducted. Testing was conducted on three brands of Latex condoms (Trojan, Durex, Lifestyles) and the (b)(4) polyurethane condom. The results of these tests are acceptable and are summarized in the following table.

Parameter	Condom Name	Untreated Mean	Treated Mean	% Difference
Tensile Strength (MPa)	Trojan Latex	24.83	23.22	-3.84
	Durex Latex	27.87	23.73	-14.7
	LifeStyles Latex	20.06	22.17	-10.5
	(b)(4) Polyurethane	26.5	26.16	-1.30
Elongation at Break (%)	Trojan Latex	709.9	703.1	-0.96
	Durex Latex	778.2	779	1.04
	LifeStyles Latex	736.9	752	2.38
	(b)(4) Polyurethane	422.11	443.62	5.36
Breaking Force (N)	Trojan Latex	86.01	82.13	-1.82
	Durex Latex	58.99	60.6	2.72
	LifeStyles Latex	64.19	70.8	10.3
	(b)(4) Polyurethane	33.13	32.76	-1.11

The sponsor was asked to address condom compatibility following lubricant exposure to the applicator. Rather than conduct additional testing, the sponsor elected to state in the labeling that when used with condoms, the lubricant should be applied directly rather than with the applicator. Please see Addendum – Sponsor Response to December 21, 2007 AI Letter – Question 2 for more detail.

Mouse Embryo Assay (MEA)

MEA is conducted to assess the potential toxicity of materials used in assisted reproduction devices to gametes and/or embryos. In order for a lubricant to be viewed as non-toxic, a minimum 86% of oocytes must develop normally following exposure.

(b)(4) lubricant was found to have no effect on the development of a 2 cell embryo at 24 hours to a blastocyst at 96 hours compared to a control. Ninety five percent of the embryos developed into blastocysts after exposure to the predicate lubricant. The results of this test are acceptable.

Bovine In-Vitro Fertilization & Embryo Development (bIVF)

bIVF is used to evaluate the effect of lubricants on sperm prior to and during the fertilization process. For example, bIVF can show inferior embryo development resulting from fertilization by sperm that had damaged DNA, although fertilization itself was normal. Lubricants should cause no greater than a 15% drop of oocytes fertilized and development of blastocysts compared to the control medium.

There was no statistically significant difference between (b)(4) lubricant and the control medium in terms of effect on fertilization or embryo development. Fertilization occurred at 77% frequency with the control medium, compared to 73% with the (b)(4) lubricant. Embryonic development occurred at 44% frequency, compared to 47% frequency with the (b)(4) lubricant. The results of this test are acceptable.

Sperm Motility Assay (Sperm/Lubricant Interaction Study)

The sperm motility assay was conducted to evaluate the direct effects of pure lubricant on sperm in semen. Sperm penetration and survival was assessed through visual observation.

Sperm was found to swim readily into and through the (b)(4) lubricant, and dissipate into it over time. In contrast, sperm did not penetrate through other leading lubricants, including FemGlide and KY Jelly. The results of this test are acceptable.

Sperm Chromatin Structure Assay

This study was conducted to evaluate sperm chromatin integrity following contact with a lubricant. Levels of DNA damage in sperm exposed to lubricant cultures should maintain 85% or more of the level of sperm DNA damage seen in control media without a lubricant.

The (b)(4) lubricant was found to not cause a significant decrease in chromatin integrity compared to the control. The control media had a percent DNA fragmentation index (%DFI) of 14.8%, while the predicate lubricant had a %DFI of 15.5%. The results of this test are acceptable.

In-Vitro Fertilization & Embryo Development

This test was conducted at the request of the FDA (b)(4) to evaluate the effects of undiluted lubricant on sperm samples ability to penetrate and fertilize an oocyte, with continued follow-up to assess embryo development.

Sperm exposed to the (b)(4) were found to have no significant difference from the control sperm (no exposure to lubricant) in their ability to fertilize oocytes or support embryonic development. The results of this test are acceptable.

The above described tests adequately show that the subject lubricant is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process. The evaluation of these tests was conducted using, "General comments on Docket No. 2003N-0539, OTC Designation for Vaginal Lubricants, Need for improved labeling for use of vaginal lubricants by trying-to-conceive couples." This document was written by JE Ellington and GD Clifton and was provided by Dr. Michael Bailey, OGDB Biologist, for determination of the type of testing needed for the indicated use of Pre~Va vaginal lubricant and the evaluation of this testing.

XII. Performance Testing – Animal

This section does not apply to this submission.

XIII. Performance Testing – Clinical

This section does not apply to this submission.

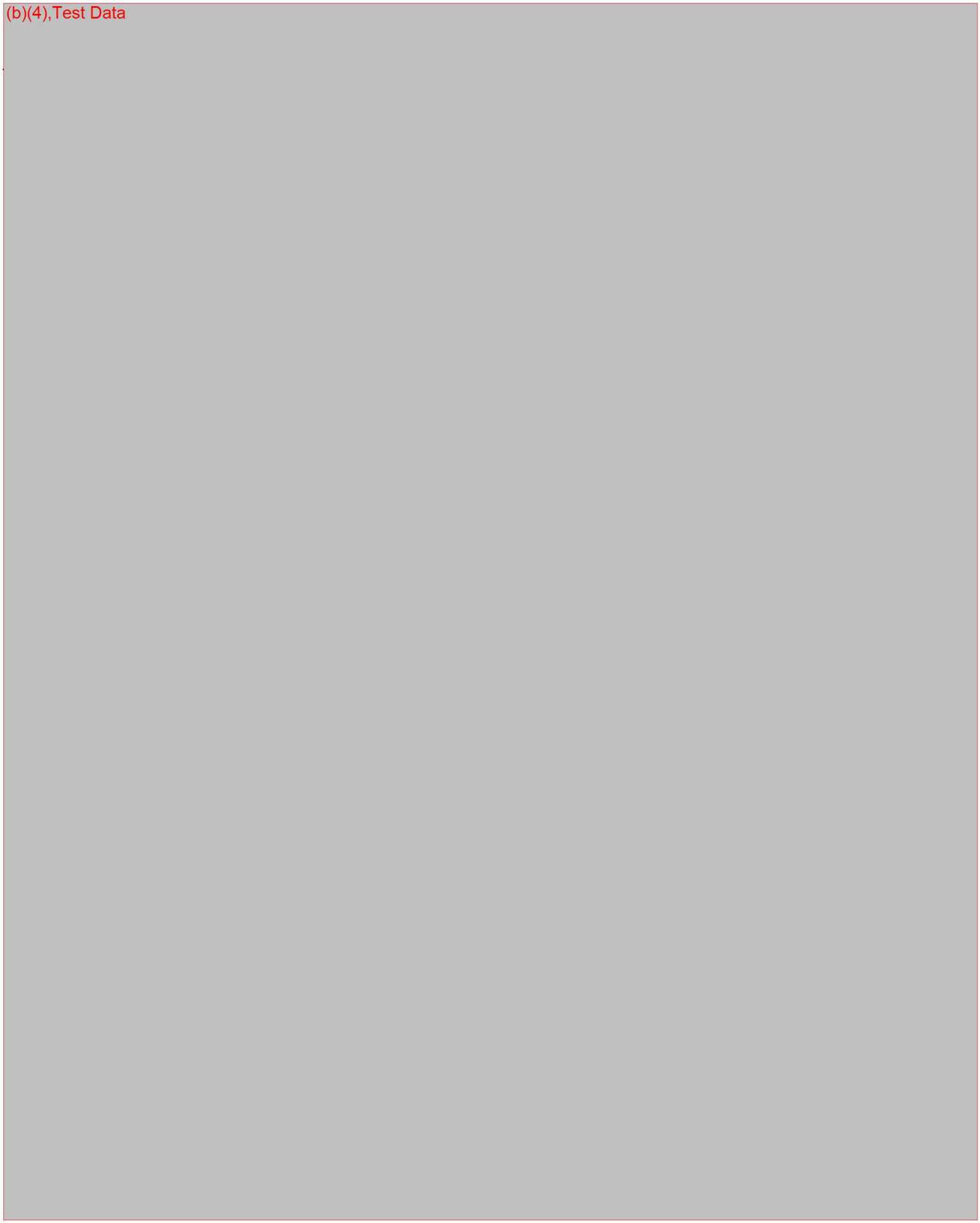
XIV. Sponsor Response to April 25, 2008 AI Letter

1. (b)(4) following testing was conducted on (b)(4) rabbit vaginal irritation, rabbit penile irritation, human skin sensitization, and slug mucosal irritation. The (b)(4) lubricant did not induce any irritation or sensitization reactions in the animals or human subjects. (b)(4) (b)(4)

   However, you have not provided the results of systemic toxicity testing (b)(4) (b)(4) This information is necessary to assess if repeated use of this product may cause absorption into the vaginal mucosal tissue and possibly cause systemic effects. Please provide the complete protocol and results of systemic toxicity testing for review.

   If you believe that systemic toxicity testing is not necessary for clearance of this lubricant, please provide justification for your decision.

The sponsor has provided systemic toxicity testing of the Pre~Va Vaginal Lubricant as requested. The testing was conducted in accordance with ISO 10993-11: Biological Evaluation of Medical


(b)(4),Test Data

The sponsor's justification regarding the test dosage as reflective of a worst case scenario was discussed in a meeting between Dr. Bailey, Dr. Alison Cotterell, OGDB Microbiologist, and myself on July 14, 2008. (b)(4) (b)(4) (b)(4) We believe that the sponsor has adequately justified that the test dosage is reflective of a worst case scenario.

In addition, the sponsor was asked to provide a summary of complaint data on the Pre' lubricant, the (b)(4) The sponsor states that since Pre' went out on the market in January 2007 (b)(4) have been sold, and zero complaints have been received from either consumers or health care professionals.

The sponsor has sufficiently addressed this question.

2. In response to Question 5 of our AI letter dated December 21, 2007, regarding the biocompatibility of the applicator to be marketed with Pre~Va lubricant, you provided the following information:

   a) Technical Data Sheets on (b)(4)
   b) Drug Master File Access Letter for (b)(4)
   c) Statement of Compliance to California's Proposition 65
   d) Compliance to CONEG Model Legislation
   e) MEM Elution Assay for cytotoxicity

   This information is not sufficient to establish the biocompatibility of the applicator for its use with Pre~Va lubricant. Although Item E demonstrates the non-cytotoxic effect of the applicator, Items A-D, while helpful in establishing the safety of the applicator in general, do not specifically address its sensitization or irritation potential. Therefore, additional biocompatibility testing should be conducted to address these issues.

   As previously stated in our AI letter, we expect that biocompatibility testing will be conducted on the final version of the applicator after exposure to Pre~Va lubricant in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, in addition to the cytotoxicity testing already provided, sensitization and irritation tests should also be conducted. Per ISO 10993, sensitization testing should include either maximization or mouse local lymph node assay tests, and vaginal irritation testing should be completed to assess irritation. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

   In lieu of testing, you may also consider contacting the applicator vendor and/or the applicator resin vendor to investigate if the applicator material is used to manufacture other products with a similar type and duration of patient contact. You will need to provide evidence that the material used for these other products is identical to that used for the proposed applicator and has a history of safe use.

The sponsor chose to submit documentation from the applicator vendor, (b)(4), stating the material used for the applicator is identical to vaginal applicators used for other products, and that the applicators also have similar type and duration of patient contact and have a history of safe use.

The sponsor submitted a letter from (b)(4), (b)(4) states that the resin used to manufacture the applicator is identical to other intravaginal applicators manufactured by (b)(4) in terms of materials, methods of manufacture, and end user function. He also states that the resin material has been used to manufacture intravaginal

applicators (b)(4) and no reports of irritation or sensitization have been reported associated with its use.

Other marketed products that use the proposed applicator are (b)(4) (b)(4) that for some products the applicator may be reused after washing with soap and warm water. For the current submission, as stated in the labeling, the applicator should be discarded after one use.

I believe that the information provided by (b)(4) is sufficient to establish the biocompatibility of the applicator. (b)(4) has shown that the resin used to manufacture the proposed applicator has been used in other intravaginal applicators with similar type and duration of contact. The sponsor has adequately addressed this question.

3. Please note that if you do not provide sufficient testing or justification to the biocompatibility issues raised, you will be asked to remove the following statement from the indications for use, "Pre~Va may be deposited intravaginally using the applicator."

The sponsor has provided sufficient justification for the biocompatibility issues raised, and therefore, may state in the indications for use that the subject lubricant may be deposited with an applicator.

XV. Substantial Equivalence Discussion

	Yes	No	
1. Same Indication Statement?		X	If **YES** = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?		X	If **YES** = Stop **NSE**
3. Same Technological Characteristics?	X		If **YES** = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If **YES** = Go To 6
5. Descriptive Characteristics Precise Enough?		X	If **NO** = Go To 8 If **YES** = Stop **SE**
6. New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NSE**
7. Accepted Scientific Methods Exist?			If **NO** = Stop **NSE**
8. Performance Data Available?	X		If **NO** = Request Data
9. Data Demonstrate Equivalence?	X		Final Decision: SE

1. Explain how the new indication differs from the predicate device's indication:

The new indication states that Pre~Va vaginal lubricant is safe to use for couples who are trying to conceive and may be deposited intravaginally using an applicator.

2. Explain why there is or is not a new effect or safety or effectiveness issue:

The safety and effectiveness issues raised have been previously addressed with fertility treatments and vaginal applicators.

5. Explain how descriptive characteristics are not precise enough:

Descriptive characteristics are not precise enough to evaluate lubricant and applicator biocompatibility, condom compatibility, and embryo fertilization and development.

9. Explain how the performance data demonstrates that the device is or is not substantially equivalent

Performance data is demonstrates that the lubricant and applicator are biocompatible, condom compatible, and do not affect embryo fertilization and development.

XVI. Deficiencies

The sponsor has resolved all remaining deficiencies.

XVII. Contact History

On May 16, 2008, the sponsor contacted me via e-mail and asked for feedback regarding their proposed protocol for systemic toxicity testing. The sponsor and myself exchanged a series of e-mails regarding this issue until June 10, 2008.

The sponsor was contacted via e-mail on July 11, 2008 regarding the systemic toxicity testing conducted. The sponsor responded on July 14, 2008 with the requested information.

The sponsor was contacted again via e-mail on July 14, 2008 regarding systemic toxicity testing. The sponsor responded on the same day with the requested information.

XVIII. Recommendation

Substantially Equivalent.

Sharon Andrews
Reviewer

7/15/08
Date

Colin M Pollard
Branch Chief

7/15/08
Date

Addendum

Sponsor Response to December 21, 2007 AI Letter

Bench Testing

1. In this submission, you state that Pre~Va will be supplied with an applicator that may be used to deposit the lubricant intravaginally. However, you have not provided any information to assess the compatibility of the applicator with the lubricant. This information is needed to ascertain if any unfavorable interactions may occur between the applicator and the lubricant that will affect the safety of this device for use by couples who are trying to conceive. Please determine if Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator. Your determination of compatibility should take into account both the duration and the environmental conditions (i.e. temperature) of lubricant exposure to the applicator during both normal and exaggerated use conditions.

   Please note that if you are unable to show that Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator, you will not be able to market the applicator for use with the lubricant.

To address this deficiency, the sponsor has provided a variety of data to assess that interactions between the applicator and the lubricant do not affect the safety of the device.

The sponsor provided the following data from the applicator vendor:

a) **Technical Data Sheets on** (b)(4)

   These data sheets provide a very general overview of the resin's mechanical properties. They also state that the resin is in compliance with 21 CFR 177.1520. They do not contain any biocompatibility information.

b) **Drug Master File Access Letter for** (b)(4)
   The Drug Master File (DMF) for (b)(4) **provides the resin specifications. It also states that the resin is in compliance with good manufacturing practices for indirect food additives. It does not contain any biocompatibility information.**

c) **Statement of Compliance to California's Proposition 65**

   California has developed a list of chemical substances which are "known to the State to cause cancer or reproductive toxicity." The sponsor has provided a letter from the resin manufacturer stating that based upon the criteria set forth in Proposition 65, the resin used to manufacture the applicator does not require a warning statement.

d) **Compliance to CONEG Model Legislation**

   The sponsor has also provided a letter from the resin manufacturer stating that the resin used to manufacture the applicator complies with CONEG Model legislation regarding heavy metals content. The sum concentrations of lead, mercury, cadmium, and hexavalent chromium in the resin are less than 100 ppm by weight.

The data provided by the applicator vendor is helpful in establishing the safety of the applicator in general, but not specifically for its use with the lubricant.

(b)(4)

(b)(4) (b)(4) . The sponsor has provided the specifications sheet and certification of the container resin (b)(4) for review. (b)(4) (b)(4) (b)(4) However, both specifications sheets state that the respective resins are in compliance with 21 CFR 177.

In addition, testing conducted on the predicate device to establish the stability of the product has demonstrated that the physical properties and gamete/embryo safety profile have not changed. This included the following testing:

a) (b)(4)
b)
c)
d)

The results of this testing were found to be acceptable. For more detail, please see Section VII – Sterilization/Shelf-Life/Reuse.

The sponsor has also provided the results of additional testing to support that after exposure to the applicator, the lubricant does not become toxic to sperm, oocytes and/or developing embryos and does not interfere with the fertilization process. Testing was conducted as previously described in Section XI – Performance Testing – Bench.

For each test, the applicator was exposed to the lubricant for (b)(4) . The sponsor states that under typical use conditions, the lubricant will be exposed to the applicator for (b)(4) . Baseline values (no exposure) were also collected. (b)(4) (b)(4) (b)(4) . This is acceptable.

a) Sperm Motility Assay

The results of this study showed that exposure to the applicator (b)(4) (b)(4) has no statistically significant effect on progressive sperm motility compared to the baseline.

b) Mouse Embryo Assay (MEA)

The results of this testing showed that following lubricant exposure to the applicator for (b)(4) did not affect embryo development compared to the control (no lubricant).

c) Bovine In Vitro Fertilization and Embryo Development (bIVF)

The results of this testing showed that exposure to the applicator at (b)(4) (b)(4) did not affect in vitro fertilization of bovine embryos or their subsequent development compared to the control (no lubricant). However, the percentage of developing embryos tended to be less after (b)(4) of exposure to the applicator.

d) Bovine Cervical Mucus Penetration

The results of this testing showed that bovine cervical mucus penetration is not affected by exposure to the applicator for (b)(4) , but decreases following exposure to the applicator for (b)(4)

The sponsor states that they cannot determine if the decrease after (b)(4) is because of exposure to the lubricant or exposure to the atmosphere. (b)(4) (b)(4) (b)(4) Based upon the results of this testing, the sponsor has developed mitigating labeling. The directions for both the personal use and clinical use sections now include the following precautions:

> **"Do not store lubricant in applicator for more than 30 minutes prior to use."**
>
> **"Keep cap tightly applied to Pre~Va tube between uses."**

This question was discussed with Dr. Bailey. Considering all of the information provided by the sponsor as a whole, the applicator can be considered non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process. The additional labeling precautions provided by the sponsor will help ensure the applicator will be used under proper conditions. The sponsor has sufficiently addressed this question.

2. Please also determine if Pre~Va remains compatible with both latex and polyurethane condoms after contact with the applicator.

   Please note that if you are unable to show that Pre~Va is compatible with both latex and polyurethane condoms after contact with the applicator, you will not be able to market the applicator for use with the lubricant, or you will have to remove the claim of "compatible with latex and polyurethane condoms" from the product labeling.

The sponsor has decided to address this issue by adding an additional section to the labeling titled "Use with Condoms." This section contains the following instructions:

> **"For use with condoms apply lubricant directly from tube. Add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface. For semen collection, only polyurethane condoms should be used."**

The sponsor's suggested labeling change is sufficient to address this question.

However, in order to validate the statement, "for semen collection, only polyurethane condoms should be used," the sponsor has conducted additional condom compatibility testing using polyurethane condoms after exposure to the applicator (b)(4) (b)(4) samples of the (b)(4) polyurethane condom were tested for tensile strength, elongation at break, and breaking force and compared to untreated samples. The results of condom compatibility testing are acceptable and summarized below.

Parameter	Untreated Mean	Treated Mean	% Difference
Tensile Strength (MPa)	29.84	28.52	-2.73
Elongation at Break (%)	475.52	465.42	-1.83
Breaking Force (N)	40.78	38.06	-1.29

This question was discussed with Dr. Bailey. The sponsor has sufficiently addressed this question.

3. You have qualitatively assessed sperm motility after contact with Pre~Va vaginal lubricant and sperm penetration through Pre~Va via visual observation. However, you have not provided a quantitative assessment of sperm motility, which is necessary to objectively determine the effect of Pre~Va vaginal lubricant on sperm motility and velocity parameters. Please provide the complete test protocols, results, and conclusions from this testing.

If you believe that quantitative analysis of sperm motility is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient, you will be asked to conduct quantitative sperm analysis.

The sponsor conducted computer assisted sperm analysis (CASA), which allows for quatification of sperm velocity and motion parameters. (b)(4)

(b)(4)

Sperm exposed to Pre~Va had a higher LIN and STR, but lower ALH and VLC. There was no statistically significant difference between VAP and VSL between the control and treated samples.

(b)(4)

The sponsor further states that CASA is used to supplement subject sperm motility and is not part of best practice guidelines for fertility evaluations as stated by ASRM. This is because normal CASA values for fertile men and their relationship to pregnancy is still a topic of debate.

The results of this testing were discussed with Dr. Bailey. He states that the forward motion of sperm is more important when assessing fertility outcomes, and that differences observed after exposure to Pre~Va are acceptable. The sponsor has sufficiently addressed this question.

4. You have not provided the results of cervical mucosal penetration testing for the Pre~Va vaginal lubricant. The results of this testing is necessary to determine that the use of Pre~Va vaginal lubricant has no detrimental effect on sperm penetration into the cervical mucous membrane. This testing may be done as either a post-coital test in human subjects or in an animal cervical mucosal model. If you choose to conduct testing on an animal model, please justify the use of the animal model that you select.

   If you believe that cervical mucosal testing is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient you will be asked to complete cervical mucosal testing.

The sponsor elected to conduct bovine cervical mucosal penetration testing. (b)(4)

(b)(4)

In this study, penetration of cryopreserved bull sperm into columns of cow estrus cervical mucus were observed following no exposure to the lubricant and following exposure to Pre~Va. (b)(4) **There was statistical difference in sperm density at 1 cm or 4 cm following exposure to Pre~Va compared to the control.**

The results of this testing were discussed with Dr. Bailey. The sponsor has sufficiently addressed this question.

Biocompatibility

5. You state in your submission that the resin utilized for the applicator is in accordance with 21 CFR 177.1520. This regulation describes "substances for use as basic components of single and repeated use food contact surfaces," and therefore, it does not apply to the applicator as it is intended to be used with the Pre~Va vaginal lubricant.

As a result, you have not provided sufficient information in this submission regarding the biocompatibility of the applicator. Please provide the complete test protocols, results, and conclusions of this testing.

We expect that biocompatibility testing will be conducted on the final, sterilized version of the device after exposure to Pre~Va lubricant in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation tests should be conducted. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

If you believe that biocompatibility testing is not necessary for clearance of this device, please provide justification for your decision. Please note that if your justification is not sufficient, you will be asked to conduct biocompatibility testing.

In order to assess the biocompatibility of the applicator, the sponsor has provided the following information:

a) **Technical Data Sheets on** (b)(4)

b) **Drug Master File Access Letter for** (b)(4)

c) **Statement of Compliance to California's Proposition 65**

d) **Compliance to CONEG Model Legislation**

e) (b)(4) **Assay for cytotoxicity**

(b)(4)

(b)(4) **The results of this study show that the applicator has no cytotoxic effect.**

Items a-d have been described previously in Question 1.

This question was discussed with Dr. Bailey. The biocompatibility information presented here is not sufficient. While items a-d help establish the biocompatibility of the applicator in general, the sensitization and irritation potential of the applicator has not been addressed as requested. The sponsor will be asked to conduct additional biocompatibility testing.

Sterilization/Packaging/Shelf-Life

6. You have not provided any information in this submission regarding the sterilization, packaging, or shelf-life of the applicator. Please provide the following information regarding the applicator.

    a. Describe the method and procedure of sterilization. If the applicator is not provided sterile, justify why sterilization is not necessary for the device as it is intended to be used.

    The applicator will not be provided sterile, and no instructions will be provided for sterilization of the applicator. The sponsor states that for the majority of clinical uses and personal use, sterilization is not necessary. However, for procedures in which sterile lubricant is required (i.e. intrauterine insemination, embryo transfer), the sponsor has provided an additional statement in the product labeling for clarification for the clinician. This statement reads as follows:

"The applicators provided in this package are not sterile. Intravaginal deposition of sterilized lubricant should be performed using a sterile instrument."

The sponsor has sufficiently addressed this deficiency.

b. Describe how the applicator will be packaged. If the applicator is provided sterile, describe how the packaging maintains device sterility.

Sets of three applicators will be packaged inside sealed, clear (b)(4) bags. Two packages of applicators will be provided with each tube of lubricant. The packaging does not need to maintain sterility because the applicators are not provided sterile. The sponsor has sufficiently addressed this deficiency.

c. Provide a shelf-life for the applicator, and describe in detail how this shelf-life was determined. The shelf-life of the applicator should meet or exceed the two year shelf life of the lubricant.

The sponsor states that (b)(4) shelf-life of the lubricant. The sponsor consulted with (b)(4), the manufacturer of applicators to obtain this information. (b)(4) states that dosage marking life expectancy validation was completed. (b)(4 compared product produced in 2003. (At the time of testing, these applicators had a manufacturing date of one year or less.) These applicators were compared to applicators produced in 1984 for dosage accuracy. Dosage accuracy had to be between ±10% accuracy. All dosage testing was found to be in compliance. (b)(4) states that this proves that the dosing accuracy does not deteriorate over time when stored at normal environmental conditions (room temperature).

For the use described in this submission, dosage accuracy is not of much, if any, importance. For both the personal and clinical uses described, the amount of lubricant used does not affect the intended use of the device. Therefore, the dosage accuracy validation described here is not relevant. However, I believe we can safely assume that the shelf-life of the applicator does exceed the shelf-life of the lubricant. The applicator is provided non-sterile and is composed of LDPE. Typically, this type of plastic materials can last an excess of five years before any discoloration is observed. This deficiency has been resolved.

Indications for Use

7. Please note that if you do not provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies, you will be asked to remove the following statement(s) from the indications for use, "Pre~Va is safe for use by couples trying to conceive," and/or "Pre~Va may be deposited intravaginally using the applicator."

As described previously, the sponsor has provided sufficient data to substantiate the first statement; however, the sponsor still needs to fully assess applicator biocompatibility. The sponsor will be told that the statement, "Pre~Va may be deposited intravaginally using the applicator," may only be included once they have fully addressed the applicator biocompatibility concerns.

8. Your indications for use statement contains the following statement, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of a medical device." Please rephrase this statement to read as follows, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions." Your indications for use page and 510(k) summary page should be updated accordingly.

Please note that as state previously, this change will only be necessary if you provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies.

The sponsor has modified the indications for use statement as recommended. An updated indication for use page and 510(k) summary has been provided. The sponsor has sufficiently addressed this question.

Labeling

9. The principle display front of the package labeling contains the following statement, "Clinically Tested and Doctor Recommend." However, you have not provided any data in this submission to support this claim. Please provide data to sufficiently justify this claim, or please remove this claim from the labeling.

   In addition, if you sufficiently justify this claim, please rephrase this claim to read as follows, "Clinically Tested and Doctor Recommended."

The sponsor has removed the claim "Clinically Tested and Doctor Recommend" from the product labeling. The sponsor has sufficiently addressed this deficiency.

10. In your submission, the applicator is described as disposable; however, the instructions for use contain do not describe how to dispose of the applicator after use. In order to avoid reuse of the applicator, please add the following statement to the end of the instructions for use on the package labeling, lubricant tube, and the package insert, "The applicator is single use only. Dispose applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."

The sponsor has slightly modified the recommended statement to read as follows:

> **"The applicator is single use only. Dispose of each applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."**

This statement has been placed on the package labeling, lubricant tube, and package insert. The sponsor has sufficiently addressed this deficiency.

11. Please place the storage conditions for the Pre~Va vaginal lubricant on the lubricant tube labeling.

The storage conditions for the device (59°F - 86°F) have been added to the lubricant tube. The sponsor has sufficiently addressed this deficiency.

Andrews, Sharon M

From: Dennis Clifton [dclifton@ingfertility.com]
Sent: Monday, July 14, 2008 6:16 PM
To: Andrews, Sharon M
Subject: RE: K072741/S2 - Pre~Va Vaginal Lubricant

Dear Dr. Andrews,

Each of the animals in the systemic toxicity study was dosed (b)(4)

I contacted the contractor and they have verified that my response is correct.

Please let me know if I may be of further assistance.

Sincerely,

Dennis

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

From: Andrews, Sharon M [mailto:sharon.andrews@fda.hhs.gov]
Sent: Monday, July 14, 2008 12:20 PM
To: Dennis Clifton
Subject: RE: K072741/S2 - Pre~Va Vaginal Lubricant

Dear Dr. Clifton,

Thank you for your prompt response. I have one additional question regarding the dosing of the animals in the systemic toxicity study.

Please clarify if the animals were dosed individually by their weight, or if the average weight of the animals was calculated and then used to determine the dose for all the animals. If the average weight was used, please specify it.

In order to complete the review of this submission in a timely manner, please provide a response to the above issues no later than **COB, Tuesday, July 15, 2008**.

Thank you.

Sharon

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB

9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850
Phone: 240-276-4148
Fax: 240-276-4156
sharon.andrews@fda.hhs.gov

From: Dennis Clifton [mailto:dclifton@ingfertility.com]
Sent: Monday, July 14, 2008 1:27 AM
To: Andrews, Sharon M
Subject: RE: K072741/S2 - Pre~Va Vaginal Lubricant

Dear Dr. Andrews,

Thank you for providing us the opportunity to further respond to your questions regarding the systemic toxicity testing of Pre~Va. Please see the attached document which further clarifies the systemic toxicity testing of Pre~Va, and provides complaint information about Pre' Lubricant.

Please contact me if you have any further questions.

Sincerely,

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

From: Andrews, Sharon M [mailto:sharon.andrews@fda.hhs.gov]
Sent: Friday, July 11, 2008 11:16 AM
To: Dennis Clifton
Subject: K072741/S2 - Pre~Va Vaginal Lubricant

Dear Dr. Clifton,

We received your response to our April 25, 2008 letter requesting additional information regarding the biocompatibility of the Pre~Va Vaginal Lubricant. We have some additional questions regarding the systemic toxicity testing you completed. Please address the following:

1. You state that normal human exposure of the Pre~Va lubricant is (b)(4). This is based on a lubricant dose of (b)(4) a 60 kg female (median weight of a 25 year old female). You also state that (b)(4) is (b)(4), and that with typical use, the lubricant would only be deposited intravaginally once per day.

   However, we believe that systemic toxicity testing should be completed using a worst case dose (e.g. use of excess lubricant, multiple uses in one day, use over many days).

Please justify how the systemic toxicity testing you completed is reflective of a worst case dosage situation.

2. In order to supplement the biocompatibility testing that you have provided, please provide a summary of any consumer complaints you may have received regarding the Pre~Va lubricant's predicate, Pre' Vaginal Lubricant.

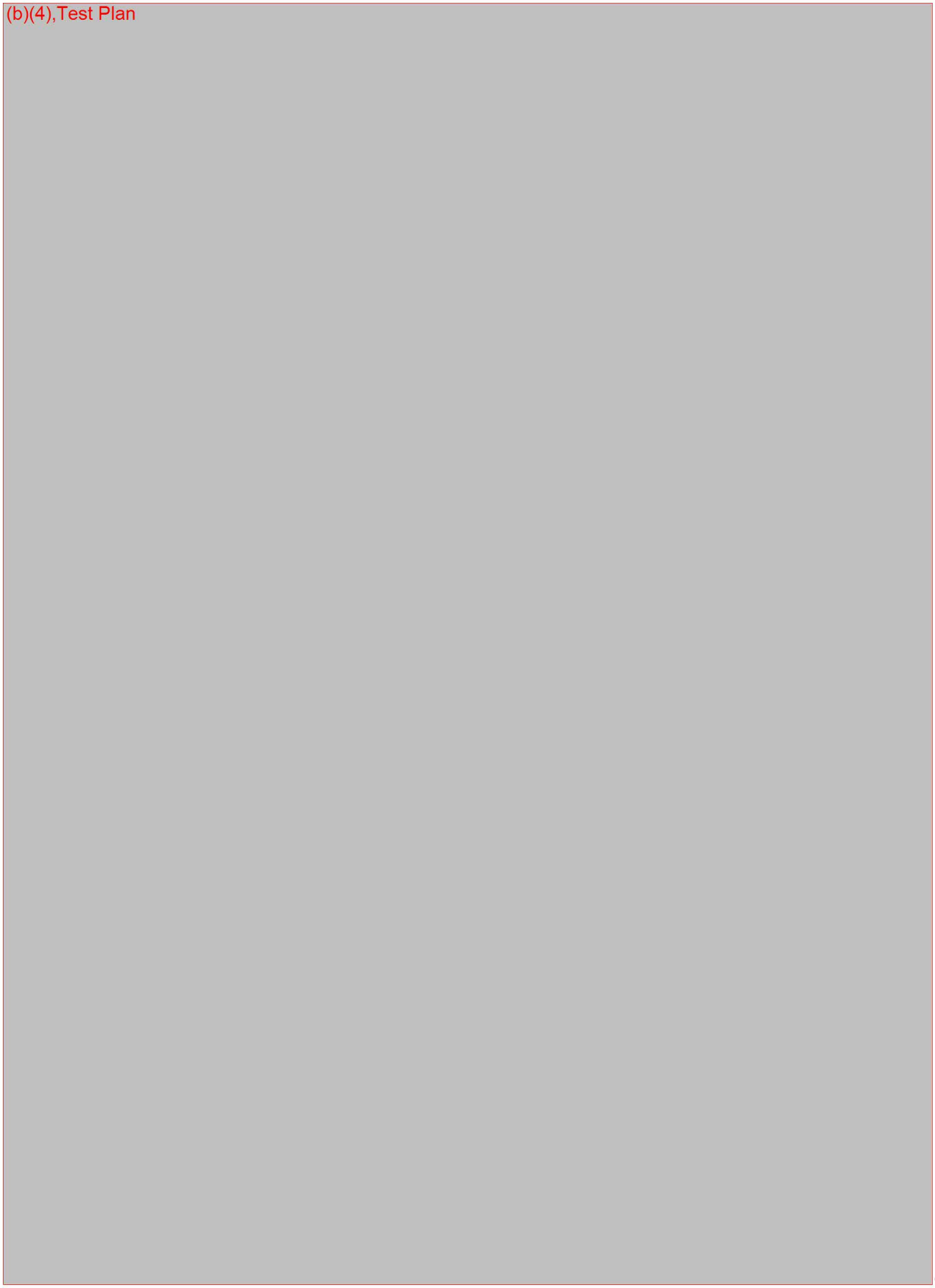
In order to complete the review of this submission in a timely manner, please provide a response to the above issues no later than **COB, Monday, July 14, 2008**.

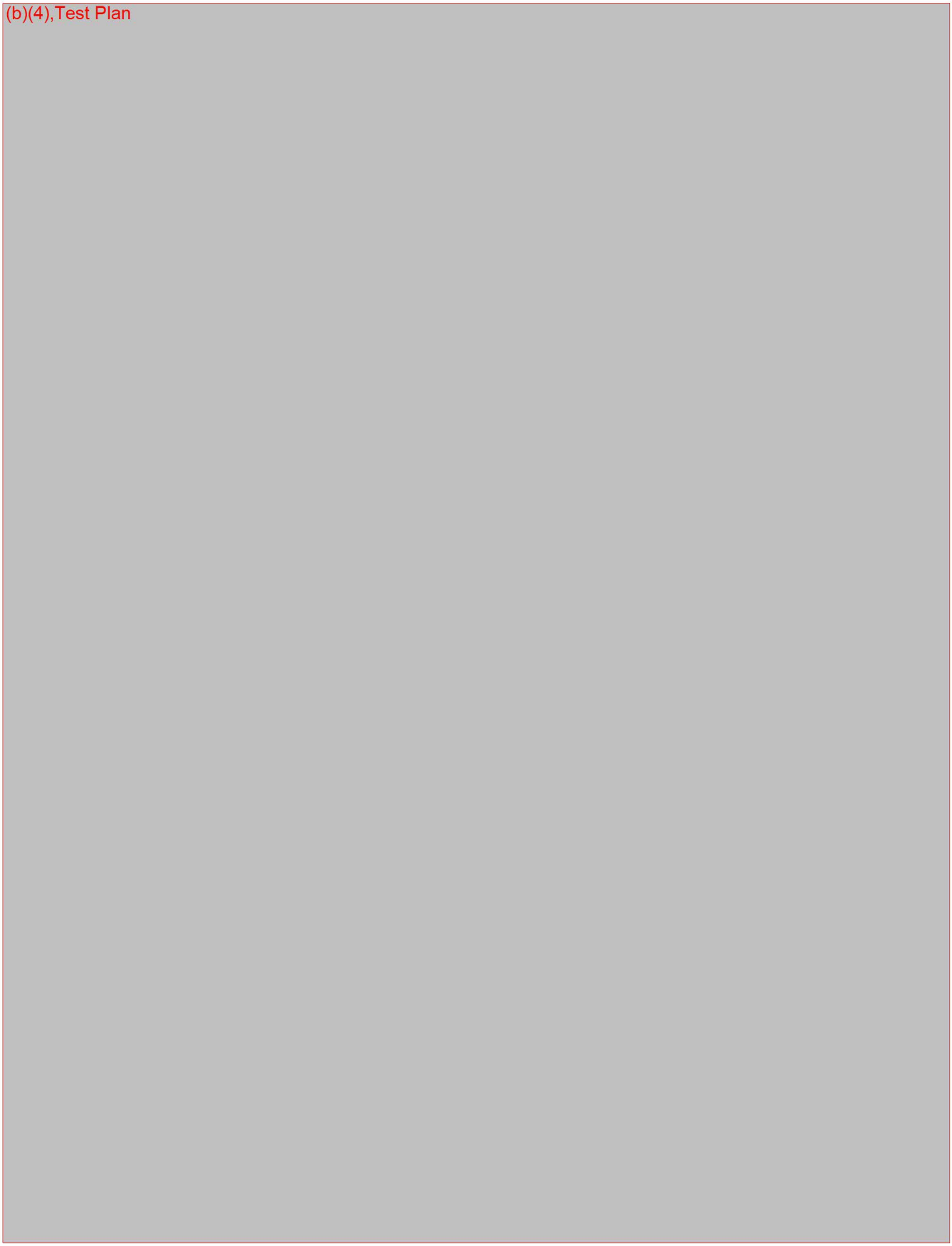
Thank you.

Sincerely,

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB
9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850
Phone: 240-276-4148
Fax: 240-276-4156
sharon.andrews@fda.hhs.gov

INGfertility




(b)(4),Test Plan


(b)(4),Test Plan

Andrews, Sharon M

From: Dennis Clifton [dclifton@ingfertility.com]
Sent: Tuesday, June 10, 2008 2:02 PM
To: Andrews, Sharon M
Subject: RE: K072741 - acute systemic toxicity

Hi Sharon,

(b)(4)

Dennis

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

From: Andrews, Sharon M [mailto:sharon.andrews@fda.hhs.gov]
Sent: Monday, June 09, 2008 12:05 PM
To: Dennis Clifton

Subject: RE: K072741 - acute systemic toxicity

Dear Dr. Clifton,

(b)(4)

Thank you,
Sharon

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB
9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850
Phone: 240-276-4148
Fax: 240-276-4156
sharon.andrews@fda.hhs.gov

From: Dennis Clifton [mailto:dclifton@ingfertility.com]
Sent: Wednesday, May 21, 2008 2:43 PM
To: Andrews, Sharon M
Cc: 'Thor S. Rollins'
Subject: RE: K072741 - acute systemic toxicity

Dear Dr. Andrews,

(b)(4)

Sincerely,

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

From: Andrews, Sharon M [mailto:sharon.andrews@fda.hhs.gov]
Sent: Tuesday, May 20, 2008 6:29 AM
To: Dennis Clifton
Subject: RE: K072741 - acute systemic toxicity

Dear Dr. Clifton,

The protocol that you have provided is a general purpose protocol, and not specific for the Pre~Va lubricant. It would be helpful if you could provide more specific detail as to how the lubricant will be administered to the test animals. In addition, the test lubricant (b)(4)

Thank you.

Sincerely,

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB
9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850
Phone: 240-276-4148
Fax: 240-276-4156
sharon.andrews@fda.hhs.gov

From: Dennis Clifton [mailto:dclifton@ingfertility.com]
Sent: Friday, May 16, 2008 5:44 PM
To: Andrews, Sharon M
Subject: K072741 - acute systemic toxicity

Dear Dr. Andrews –

We are preparing to perform an acute systemic toxicity test of the Pre~Va lubricant as requested in your most recent response to the 510(k) application referenced above. Attached is the basic protocol for the testing. I have two questions for you before we proceed with the testing:

1. Is protocol for testing satisfactory in your opinion?
2. We believe the most appropriate test would be (b)(4) Do you concur that this route is appropriate for testing the acute systemic toxicity of the gel?

Thank you in advance for your time and consideration.

Sincerely,

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Sharon Andrews

Subject: 510(k) Number K072741/S1

To: The Record

Please list CTS decision code A1

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/ Screening Checklist)

☑ Hold (Additional Information or Telephone Hold).

☐ Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	*Attach IFU*		
510(k) Summary /510(k) Statement	*Attach Summary*		
Truthful and Accurate Statement	*Must be present for a Final Decision*		
Is the device Class III? If yes, does firm include Class III Summary?	*Must be present for a Final Decision*		
Does firm reference standards? (If yes, please attach form from http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4136/ABBREVIATED STANDARDS DATA FORM.DOC)			
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC			
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			
Is this device intended for pediatric use only?			
Is this a prescription device? (If both prescription & OTC, check both boxes.)			
Is clinical data necessary to support the review of this 510(k)?			
Does this device include an Animal Tissue Source?			
Is this device subject to Section 522 Postmarket Surveillance? (Postmarket Surveillance Guidance, http://www.fda.gov/cdrh/osb/guidance/316.html)	*Contact OSB*		
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC*		

Regulation Number	Class*	Product Code
21 CFR 884.5300	Class II	NUC

(*If unclassified, see 510(k) Staff)

Additional Product Codes: _____

Review: Colin M. Pollard OGDB 4/23/08
(Branch Chief) (Branch Code) (Date)

Final Review: _____
(Division Director) (Date)

Rev. 5/30/07

DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
Traditional/Abbreviated

K072741/S001

Date: April 23, 2008
To: The Record
From: Sharon Andrews, Biomedical Engineer

Office: ODGB
Division: DRARD

510(k) Holder: INGfertility, LLC
Device Name: Pre~Va Vaginal Lubricant
Contact: Dennis Clifton, Pharm.D., Vice President
Address: 17206 South Spangle Creek Road, Valleyford, WA 99036
Phone: 509-443-0149
Fax: 509-471-9638
Email: dclifton@ingfertility.com

I. Purpose and Submission Summary

The 510(k) holder would like to introduce the Pre~Va vaginal lubricant into interstate commerce. Pre~Va is a personal lubricant that is compatible with both latex and polyurethane condoms. It may also be used to lubricate devices used during fertility interventions and is safe for use by couples trying to conceive. Pre~Va will also be marketed with an applicator for intravaginal deposition.

This is the second round of review of this submission. The sponsor was sent a letter requesting additional information on December 21, 2007. The sponsor has not fully assessed the biocompatibility of the lubricant or the applicator and will be asked for additional information to address these issues.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use page (OTC)	X		
Truthful and Accuracy Statement	X		
510(k) Summary or 510(k) Statement	X		
Standards Form			X

III. Device Description

	Yes	No	N/A
Is the device life-supporting or life sustaining?		X	
Is the device an implant (implanted longer than 30 days)?		X	

K072741

	Yes	No	N/A
Does the device design use software?		X	
Is the device sterile?		X	
Is the device reusable (not reprocessed single use)?		X	
Are "cleaning" instructions included for the end user?			X

The formulation of Pre~Va Vaginal lubricant, including the respective weight percent, function, and Chemical Abstracts Service (CAS) Numbers of each ingredient are listed in the table below.

Ingredient	Weight Percent (%w/w)	Function	CAS Number
Water	(b)(4)	Solvent	7732-18-5
Hydroxyethylcellulose, NF		(b)(4)	9004-62-0
Pluronic 127, NF			9003-11-6
Sodium Chloride, USP			7647-14-5
Arabinogalactan			9036-66-2
Sodium Phosphate			(b)(4)
Carbopol 934P, NF			9003-01-4
Methylparaben, USP			99-76-3
Sodium Hydroxide, NF			1310-73-2
Potassium Phosphate			(b)(4)

The specifications of Pre~Va are outlined in the following table.

Physical Specifications/Tests	Ranges/Specifications
pH @ 25°C	7.20 – 7.45
Osmolarity	260 and 360 mOsmo/kg
Apparent Viscosity	8,500 – 12,000 cps
Specific Gravity	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens; <100 cfu/ml other organisms
Endotoxin by LAL methodology	<0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA to > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility following 30 minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium

Pre~Va will be supplied with an applicator. The sponsor provided three samples of the applicator with the submission. The applicator has a piston style design and is made of (b)(4) (b)(4). The resin utilized for the applicator is in accordance with 21 CFR 177.1520, which describes "substances for use as basic components of single and repeated use food contact surfaces." This regulation is not applicable to the applicator for use with a lubricant.

The applicators are manufactured by (b)(4) The sponsor has provided engineering drawings noting the dimensions for the applicator. The fully extended length of the applicator is 8.9 inches, and the fully compressed length of the applicator is 4.9 inches. The diameter of the applicator at its widest point is 0.56 inches. The applicator is marked with the following fill lines, 0.5, 1, 2, 3, and 4 grams. The (b)(4)

The applicator can be screwed onto the lubricant tube, and the lubricant can be squeezed into the applicator to a desired amount. The applicator is disposable.

IV. Indications for Use

Pre~Va vaginal lubricant is intended to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. *Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.* As a personal lubricant, Pre~Va supplements the body's own natural lubrication fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. *Pre~Va is safe for use by couples trying to conceive* and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

V. Predicate Device Comparison

The predicate device for the subject lubricant is the Pre' vaginal lubricant, also marketed by INGFertility. Pre' vaginal lubricant is intended to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. As a personal lubricant, Pre' supplements the body's own natural lubrication fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre' may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

Pre' vaginal lubricant was cleared under 510(k) K051436 on October 13, 2006. It is classified as a condom under 21 CFR 884.5300 and procode NUC.

The intended use of the subject and predicate lubricants is not the same. The subject lubricant has an expanded indication, which is italicized above in Section IV – Indications for Use. However, the difference in the intended use does not alter the intended therapeutic or diagnostic effect.

(b)(4)

There are two primary differences between the predicate and subject lubricants: (1) the subject lubricant claims to safe to use by couples trying to conceive, and (2) the subject lubricant is packaged with a (b)(4) applicator. The consequences of these changes are discussed below in the appropriate sections of this review memo.

VI. Labeling

Labeling has been provided which includes instructions for use and an appropriate prescription statement as required by CFR 21.807.87 (e). This product will be sold over the counter.

The sponsor has provided draft labeling that will be found on the lubricant package, the lubricant tube, and a draft package insert.

The package labeling (p.36) contains the following information: product claims, directions for use (personal and clinical), ingredients, warnings, caution statements, storage information, expiration date, and lot number.

The package labeling (email dated 11/28/07) contains the following information: product claims, directions for use (personal and clinical), ingredients, warnings, caution statements, expiration date, and lot number. The sponsor will be asked to place the storage information on the lubricant tube labeling.

The package insert (p.39) contains more detailed instructions for use, warnings, caution statements, storage information, ingredients, products specifications, and validated instructions for sterilization.

The labeling for this product is acceptable.

VII. Sterilization/Shelf Life/Reuse

Pre~Va vaginal lubricant is supplied non-sterile. It is specified to have microbial limits at 48 hours of 0 cfu/ml pathogens and <100 cfu/ml other organisms. The endotoxin limit is <0.5 EU/ml. These are identical to the specifications of the predicate lubricant.

The clinical instructions for use found in the package insert provide instructions for sterilization to a SAL of (b)(4) This is for when clinics desire a sterilized product for procedures such as intrauterine insemination and embryo transfer. These instructions are identical to those supplied with the predicate lubricant.

Stability testing was conducted (b)(4)
(b)(4)
Samples were found to be within range for all intervals tested according to the table below.

Physical Specification	Acceptable Range
(b)(4)	(b)(4)

In addition, the following testing was conducted upon completion of stability testing:

a) (b)(4)
b)
c)
d)

The details of this testing are described in Section XI – Performance Testing – Bench. The results of this testing are acceptable.

The stability data collected (b)(4)
(b)(4)

The applicator will be provided non-sterile. For more information, please see Section XIV – Sponsor Response to December 21, 2007 AI Letter – Question 6.

VIII. Biocompatibility

This lubricant is a surface device that is in contact with both the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation activity tests must be completed.

The following biocompatibility testing was conducted (b)(4) : rabbit vaginal irritation, rabbit penile irritation, human skin sensitization, and slug mucosal irritation. The (b)(4) lubricant did not induce any irritation or sensitization reactions in the animals or human subjects. (b)(4) (b)(4) the results of biocompatibility testing (b)(4) are acceptable for the Pre~Va lubricant.

(b)(4) systemic toxicity testing (b)(4) This issue was discussed with Dr. Michael Bailey, OGDB Biologist, and Colin Pollard, OGDB Branch Chief. It was decided that the sponsor should be asked to conduct this testing as this is now standard lubricant review policy. Because of the repeated use nature of a lubricant, it is possible that it could be absorbed, and thus result in systemic effects.

The sponsor has also assessed the biocompatibility of the applicator, but there are some additional biocompatibility concerns remaining with the applicator. For more information, please see Section XIV – Sponsor Response to December 21, 2007 AI Letter – Question 5.

IX. Software

This section does not apply to this submission.

X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

This section does not apply to this submission.

XI. Performance Testing – Bench

Lubricant/Applicator Compatibility

The sponsor has provided testing assessing the compatibility of the lubricant and the applicator. The results of this testing are acceptable. The details of this testing can be found in Section XIV – Sponsor Response to December 21, 2007 AI Letter – Question 1.

The following testing was conducted (b)(4) (b)(4)

Condom Compatibility

Condom compatibility testing was conducted by Nelson Laboratories (Salt Lake City, UT). Results from this testing indicated the predicate lubricant was compatible with both latex and polyurethane condoms and that the use of the lubricant had no statistically significant effects on tensile strength, elongation at break, or breaking force. Burst testing was not conducted. Testing was conducted on three brands of Latex condoms (Trojan, Durex, Lifestyles) and the Apex Male Factor Pak polyurethane condom. The results of these tests are acceptable and are summarized below.

Parameter	Condom Name	Untreated Mean	Treated Mean	% Difference
Tensile Strength (MPa)	Trojan Latex	24.83	23.22	-3.84
	Durex Latex	27.87	23.73	-13.34
	LifeStyles Latex	20.06	22.17	22.1
	(b)(4) Polyurethane	26.5	26.16	-0.25
Elongation at Break (%)	Trojan Latex	709.9	703.1	-0.77
	Durex Latex	778.2	779	1.04
	LifeStyles Latex	736.9	752	2.38
	(b)(4) Polyurethane	422.11	443.62	5.36

Breaking Force (N)	Trojan Latex	86.01	82.13	-1.82
	Durex Latex	58.99	60.6	4.29
	LifeStyles Latex	64.19	70.8	19.7
	(b)(4) Polyurethane	33.13	32.76	-0.12

The sponsor was asked to address condom compatibility following lubricant exposure to the applicator. Rather than conduct additional testing, the sponsor elected to state in the labeling that when used with condoms, the lubricant should be applied directly rather than with the applicator. Please see Section XIV – Sponsor Response to December 21, 2007 AI Letter – Question 2 for more detail.

Mouse Embryo Assay (MEA)

MEA is conducted to assess the potential toxicity of materials used in assisted reproduction devices to gametes and/or embryos. In order for a lubricant to be viewed as non-toxic, a minimum 86% of oocytes must develop normally following exposure.

The (b)(4) lubricant was found to have no effect on the development of a 2 cell embryo at 24 hours to a blastocyst at 96 hours compared to a control. Ninety five percent of the embryos developed into blastocysts after exposure to the (b)(4) lubricant. The results of this test are acceptable.

Bovine In-Vitro Fertilization & Embryo Development (bIVF)

bIVF is used to evaluate the effect of lubricants on sperm prior to and during the fertilization process. For example, bIVF can show inferior embryo development resulting from fertilization by sperm that had damaged DNA, although fertilization itself was normal. Lubricants should cause no greater than a 15% drop of oocytes fertilized and development of blastocysts compared to the control medium.

There was not statistically significant difference between the (b)(4) lubricant and the control medium in terms of effect on fertilization or embryo development. Fertilization occurred at 77% frequency with the control medium, compared to 73% with the (b)(4) lubricant. Embryonic development occurred at 44% frequency, compared to 47% frequency with the (b)(4) lubricant. The results of this test are acceptable.

Sperm Motility Assay (Sperm/Lubricant Interaction Study)

The sperm motility assay was conducted to evaluate the direct effects of pure lubricant on sperm in semen. Sperm penetration and survival was assessed through visual observation.
Sperm was found to swim readily into and through the predicate lubricant, and dissipate into it over time. In contrast, sperm did not penetrate through other leading lubricants, including FemGlide and KY Jelly. The results of this test are acceptable.

Sperm Chromatin Structure Assay

This study was conducted to evaluate sperm chromatin integrity following contact with a lubricant. Levels of DNA damage in sperm exposed to lubricant cultures should maintain 85% or more of the level of sperm DNA damage seen in control media without a lubricant.

The (b)(4) lubricant was found to not cause a significant decrease in chromatin integrity compared to the control. The control media had a percent DNA fragmentation index (%DFI) of 14.8%, while the (b)(4) lubricant had a %DFI of 15.5%. The results of this test are acceptable.

In-Vitro Fertilization & Embryo Development

This test was conducted at the request of the FDA (b)(4) to evaluate the effects of undiluted lubricant on sperm samples ability to penetrate and fertilize an oocyte, with continued follow-up to assess embryo development.

Sperm exposed (b)(4) were found to have no significant difference from the control sperm (no exposure to lubricant) in their ability to fertilize oocytes or support embryonic development. The results of this test are acceptable.

The above described tests adequately show that the subject lubricant is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process. The evaluation of these tests was conducted using, "General comments on Docket No. 2003N-0539, OTC Designation for Vaginal Lubricants, Need for improved labeling for use of vaginal lubricants by trying-to-conceive couples." This document was written by JE Ellington and GD Clifton and was provided by Dr. Bailey for determination of the type of testing needed for the indicated use of Pre~Va vaginal lubricant and the evaluation of this testing.

XII. Performance Testing – Animal

This section does not apply to this submission.

XIII. Performance Testing – Clinical

This section does not apply to this submission.

XIV. Sponsor Response to December 21, 2007 AI Letter

Bench Testing

1. In this submission, you state that Pre~Va will be supplied with an applicator that may be used to deposit the lubricant intravaginally. However, you have not provided any information to assess the compatibility of the applicator with the lubricant. This information is needed to ascertain if any unfavorable interactions may occur between the applicator and the lubricant that will affect the safety of this device for use by couples who are trying to conceive. Please determine if Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator. Your determination of compatibility should take into account both the duration and the environmental conditions (i.e. temperature) of lubricant exposure to the applicator during both normal and exaggerated use conditions.

   Please note that if you are unable to show that Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator, you will not be able to market the applicator for use with the lubricant.

To address this deficiency, the sponsor has provided a variety of data to assess that interactions between the applicator and the lubricant do not affect the safety of the device.

The sponsor provided the following data from the applicator vendor:

a) Technical Data Sheets on (b)(4)

These data sheets provide a very general overview of the resin's mechanical properties. They also state that the resin is in compliance with 21 CFR 177.1520. They do not contain any biocompatibility information.

b) Drug Master File Access Letter for (b)(4)

The Drug Master File (DMF) for (b)(4) provides the resin specifications. It also states that the resin is in compliance with good manufacturing practices for indirect food additives. It does not contain any biocompatibility information.

c) Statement of Compliance to California's Proposition 65

California has developed a list of chemical substances which are "known to the State to cause cancer or reproductive toxicity." The sponsor has provided a letter from the resin manufacturer stating that based upon the criteria set forth in Proposition 65, the resin used to manufacture the applicator does not require a warning statement.

d) Compliance to CONEG Model Legislation

The sponsor has also provided a letter from the resin manufacturer stating that the resin used to manufacture the applicator complies with CONEG Model legislation regarding heavy metals content. The sum concentrations of lead, mercury, cadmium, and hexavalent chromium in the resin are less than 100 ppm by weight.

The data provided by the applicator vendor is helpful in establishing the safety of the applicator in general, but not specifically for its use with the lubricant.

(b)(4)

(b)(4) The sponsor has provided the specifications sheet and certification of the container resin (b)(4) for review. (b)(4)
(b)(4)
(b)(4) However, both specifications sheets state that the respective resins are in compliance with 21 CFR 177.

In addition, testing conducted on the predicate device to establish the stability of the product has demonstrated that the physical properties and gamete/embryo safety profile have not changed. This included the following testing:

a) (b)(4)
b)
c)
d)

The results of this testing were found to be acceptable. For more detail, please see Section VII – Sterilization/Shelf-Life/Reuse.

The sponsor has also provided the results of additional testing to support that after exposure to the applicator, the lubricant does not become toxic to sperm, oocytes and/or developing embryos and does not interfere with the fertilization process. Testing was conducted as previously described in Section XI – Performance Testing – Bench.

For each test, the applicator was exposed to the lubricant for (b)(4). The sponsor states that under typical use conditions, the lubricant will be exposed to the applicator for (b)(4) Baseline values (no exposure) were also collected. (b)(4)
(b)(4)
(b)(4) This is acceptable.

a) Sperm Motility Assay

The results of this study showed that exposure to the applicator for (b)(4) hours has no statistically significant effect on progressive sperm motility compared to the baseline.

b) Mouse Embryo Assay (MEA)

The results of this testing showed that following lubricant exposure to the applicator for (b)(4) did not affect embryo development compared to the control (no lubricant).

c) Bovine In Vitro Fertilization and Embryo Development (bIVF)

The results of this testing showed that exposure to the applicator at (b)(4) (b)(4) did not affect in vitro fertilization of bovine embryos or their subsequent development compared to the control (no lubricant). However, the percentage of developing embryos tended to be less after (b)(4) of exposure to the applicator.

d) Bovine Cervical Mucus Penetration

The results of this testing showed that bovine cervical mucus penetration is not affected by exposure to the applicator (b)(4), but decreases following exposure to the applicator (b)(4).

The sponsor states that they cannot determine if the decrease after (b)(4) is because of exposure to the lubricant or exposure to the atmosphere. (b)(4) (b)(4) (b)(4) Based upon the results of this testing, the sponsor has developed mitigating labeling. The directions for both the personal use and clinical use sections now include the following precautions:

> **"Do not store lubricant in applicator for more than 30 minutes prior to use."**
>
> **"Keep cap tightly applied to Pre~Va tube between uses."**

This question was discussed with Dr. Bailey. Considering all of the information provided by the sponsor as a whole, the applicator can be considered non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process. The additional labeling precautions provided by the sponsor will help ensure the applicator will be used under proper conditions. The sponsor has sufficiently addressed this question.

2. Please also determine if Pre~Va remains compatible with both latex and polyurethane condoms after contact with the applicator.

   Please note that if you are unable to show that Pre~Va is compatible with both latex and polyurethane condoms after contact with the applicator, you will not be able to market the applicator for use with the lubricant, or you will have to remove the claim of "compatible with latex and polyurethane condoms" from the product labeling.

The sponsor has decided to address this issue by adding an additional section to the labeling titled "Use with Condoms." This section contains the following instructions:

> **"For use with condoms apply lubricant directly from tube. Add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface. For semen collection, only polyurethane condoms should be used."**

The sponsor's suggested labeling change is sufficient to address this question.

However, in order to validate the statement, "for semen collection, only polyurethane condoms should be used," the sponsor has conducted additional condom compatibility testing using polyurethane condoms after exposure to the applicator (b)(4) . (b)(4) samples of the (b)(4) polyurethane condom were tested for tensile strength, elongation at break, and breaking force and compared to untreated samples. The results of condom compatibility testing are acceptable and summarized below.

Parameter	Untreated Mean	Treated Mean	% Difference
Tensile Strength (MPa)	29.84	28.52	-2.73
Elongation at Break (%)	475.52	465.42	-1.83
Breaking Force (N)	40.78	38.06	-1.29

This question was discussed with Dr. Bailey. The sponsor has sufficiently addressed this question.

3. You have qualitatively assessed sperm motility after contact with Pre~Va vaginal lubricant and sperm penetration through Pre~Va via visual observation. However, you have not provided a quantitative assessment of sperm motility, which is necessary to objectively determine the effect of Pre~Va vaginal lubricant on sperm motility and velocity parameters. Please provide the complete test protocols, results, and conclusions from this testing.

   If you believe that quantitative analysis of sperm motility is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient, you will be asked to conduct quantitative sperm analysis.

The sponsor conducted computer assisted sperm analysis (CASA), which allows for quatification of sperm velocity and motion parameters. (b)(4)
(b)(4)

Sperm exposed to Pre~Va had a higher LIN and STR, but lower ALH and VLC. There was no statistically significant difference between VAP and VSL between the control and treated samples.
(b)(4)

The sponsor further states that CASA is used to supplement subject sperm motility and is not part of best practice guidelines for fertility evaluations as stated by ASRM. This is because normal CASA values for fertile men and their relationship to pregnancy is still a topic of debate.

The results of this testing were discussed with Dr. Bailey. He states that the forward motion of sperm is more important when assessing fertility outcomes, and that differences observed after exposure to Pre~Va are acceptable. The sponsor has sufficiently addressed this question.

4. You have not provided the results of cervical mucosal penetration testing for the Pre~Va vaginal lubricant. The results of this testing is necessary to determine that the use of Pre~Va vaginal lubricant has no detrimental effect on sperm penetration into the cervical mucous membrane. This testing may be done as either a post-coital test in human subjects or in an animal cervical mucosal model. If you choose to conduct testing on an animal model, please justify the use of the animal model that you select.

If you believe that cervical mucosal testing is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient you will be asked to complete cervical mucosal testing.

The sponsor elected to conduct bovine cervical mucosal penetration testing. (b)(4)

(b)(4)

In this study, penetration of cryopreserved bull sperm into columns of cow estrus cervical mucus were observed following no exposure to the lubricant and following exposure to Pre~Va. There was statistical difference in sperm density at 1 cm or 4 cm following exposure to Pre~Va compared to the control. (b)(4)

The results of this testing were discussed with Dr. Bailey. The sponsor has sufficiently addressed this question.

Biocompatibility

5. You state in your submission that the resin utilized for the applicator is in accordance with 21 CFR 177.1520. This regulation describes "substances for use as basic components of single and repeated use food contact surfaces," and therefore, it does not apply to the applicator as it is intended to be used with the Pre~Va vaginal lubricant.

   As a result, you have not provided sufficient information in this submission regarding the biocompatibility of the applicator. Please provide the complete test protocols, results, and conclusions of this testing.

   We expect that biocompatibility testing will be conducted on the final, sterilized version of the device after exposure to Pre~Va lubricant in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation tests should be conducted. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

   If you believe that biocompatibility testing is not necessary for clearance of this device, please provide justification for your decision. Please note that if your justification is not sufficient, you will be asked to conduct biocompatibility testing.

In order to assess the biocompatibility of the applicator, the sponsor has provided the following information:

a) **Technical Data Sheets on** (b)(4)

b) **Drug Master File Access Letter for** (b)(4)

c) **Statement of Compliance to California's Proposition 65**

d) **Compliance to CONEG Model Legislation**

e) (b)(4) **Assay for cytotoxicity**

(b)(4)

(b)(4) **The results of this study show that the applicator has no cytotoxic effect.**

Items a-d have been described previously in Question 1.

This question was discussed with Dr. Bailey. The biocompatibility information presented here is not sufficient. While items a-d help establish the biocompatibility of the applicator in general, the sensitization and irritation potential of the applicator has not been addressed as requested. The sponsor will be asked to conduct additional biocompatibility testing.

Sterilization/Packaging/Shelf-Life

6. You have not provided any information in this submission regarding the sterilization, packaging, or shelf-life of the applicator. Please provide the following information regarding the applicator.

   a. Describe the method and procedure of sterilization. If the applicator is not provided sterile, justify why sterilization is not necessary for the device as it is intended to be used.

   The applicator will not be provided sterile, and no instructions will be provided for sterilization of the applicator. The sponsor states that for the majority of clinical uses and personal use, sterilization is not necessary. However, for procedures in which sterile lubricant is required (i.e. intrauterine insemination, embryo transfer), the sponsor has provided an additional statement in the product labeling for clarification for the clinician. This statement reads as follows:

   "The applicators provided in this package are not sterile. Intravaginal deposition of sterilized lubricant should be performed using a sterile instrument."

   The sponsor has sufficiently addressed this deficiency.

   b. Describe how the applicator will be packaged. If the applicator is provided sterile, describe how the packaging maintains device sterility.

   Sets of three applicators will be packaged inside sealed, clear (b)(4) **bags. Two packages of applicators will be provided with each tube of lubricant. The packaging does not need to maintain sterility because the applicators are not provided sterile. The sponsor has sufficiently addressed this deficiency.**

   c. Provide a shelf-life for the applicator, and describe in detail how this shelf-life was determined. The shelf-life of the applicator should meet or exceed the two year shelf life of the lubricant.

   The sponsor states that the (b)(4) **shelf-life of the lubricant. The sponsor consulted with SRC Medical, the manufacturer of applicators to obtain this information.** (b)(4) **states that dosage marking life expectancy validation was completed.** (b)(4) **compared product produced in 2003. (At the time of testing, these applicators had a manufacturing date of one year or less.) These applicators were compared to applicators produced in 1984 for dosage accuracy. Dosage accuracy had to be between ±10% accuracy. All dosage testing was found to be in compliance.** (b)(4) **states that this proves that the dosing accuracy does not deteriorate over time when stored at normal environmental conditions (room temperature).**

   For the use described in this submission, dosage accuracy is not of much, if any, importance. For both the personal and clinical uses described, the amount of lubricant used does not affect the intended use of the device. Therefore, the dosage accuracy validation described here is not relevant. However, I believe we can safely assume that

the shelf-life of the applicator does exceed the shelf-life of the lubricant. The applicator is provided non-sterile and is composed of (b)(4) Typically, this type of plastic materials can last an excess of five years before any discoloration is observed. This deficiency has been resolved.

Indications for Use

7. Please note that if you do not provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies, you will be asked to remove the following statement(s) from the indications for use, "Pre~Va is safe for use by couples trying to conceive," and/or "Pre~Va may be deposited intravaginally using the applicator."

As described previously, the sponsor has provided sufficient data to substantiate the first statement; however, the sponsor still needs to fully assess applicator biocompatibility. The sponsor will be told that the statement, "Pre~Va may be deposited intravaginally using the applicator," may only be included once they have fully addressed the applicator biocompatibility concerns.

8. Your indications for use statement contains the following statement, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of a medical device." Please rephrase this statement to read as follows, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions." Your indications for use page and 510(k) summary page should be updated accordingly.

   Please note that as state previously, this change will only be necessary if you provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies.

The sponsor has modified the indications for use statement as recommended. An updated indication for use page and 510(k) summary has been provided. The sponsor has sufficiently addressed this question.

Labeling

9. The principle display front of the package labeling contains the following statement, "Clinically Tested and Doctor Recommend." However, you have not provided any data in this submission to support this claim. Please provide data to sufficiently justify this claim, or please remove this claim from the labeling.

   In addition, if you sufficiently justify this claim, please rephrase this claim to read as follows, "Clinically Tested and Doctor Recommended."

The sponsor has removed the claim "Clinically Tested and Doctor Recommend" from the product labeling. The sponsor has sufficiently addressed this deficiency.

10. In your submission, the applicator is described as disposable; however, the instructions for use contain do not describe how to dispose of the applicator after use. In order to avoid reuse of the applicator, please add the following statement to the end of the instructions for use on the package labeling, lubricant tube, and the package insert, "The applicator is single use only. Dispose applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."

The sponsor has slightly modified the recommended statement to read as follows:

> **"The applicator is single use only. Dispose of each applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant**

by hand."

This statement has been placed on the package labeling, lubricant tube, and package insert. The sponsor has sufficiently addressed this deficiency.

11. Please place the storage conditions for the Pre~Va vaginal lubricant on the lubricant tube labeling.

The storage conditions for the device (59°F - 86°F) have been added to the lubricant tube. The sponsor has sufficiently addressed this deficiency.

XV. Substantial Equivalence Discussion

	Yes	No	
1. Same Indication Statement?		X	If **YES** = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?		X	If **YES** = Stop **NSE**
3. Same Technological Characteristics?	X		If **YES** = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If **YES** = Go To 6
5. Descriptive Characteristics Precise Enough?		X	If **NO** = Go To 8 If **YES** = Stop **SE**
6. New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NSE**
7. Accepted Scientific Methods Exist?			If **NO** = Stop **NSE**
8. Performance Data Available?		X	If **NO** = Request Data
9. Data Demonstrate Equivalence?			Final Decision:

1. Explain how the new indication differs from the predicate device's indication:

The new indication states that Pre~Va vaginal lubricant is safe to use for couples who are trying to conceive and may be deposited intravaginally using an applicator.

2. Explain why there is or is not a new effect or safety or effectiveness issue:

The safety and effectiveness issues raised have been previously addressed with fertility treatments and vaginal applicators.

5. Explain how descriptive characteristics are not precise enough:

Descriptive characteristics are not precise enough to evaluate lubricant and applicator biocompatibility.

8. Explain what performance data is needed:

Performance data is needed to evaluate lubricant and applicator biocompatibility.

XVI. Deficiencies

1. (b)(4) (b)(4) The following testing was conducted (b)(4) rabbit vaginal irritation, rabbit penile

irritation, human skin sensitization, and slug mucosal irritation. The (b)(4) lubricant did not induce any irritation or sensitization reactions in the animals or human subjects. (b)(4) (b)(4)

However, you have not provided the results of systemic toxicity testing (b)(4) (b)(4) This information is necessary to assess if repeated use of this product may cause absorption into the vaginal mucosal tissue and possibly cause systemic effects. Please provide the complete protocol and results of systemic toxicity testing for review.

If you believe that systemic toxicity testing is not necessary for clearance of this lubricant, please provide justification for your decision.

2. In response to Question 5 of our AI letter dated December 21, 2007, regarding the biocompatibility of the applicator to be marketed with Pre~Va lubricant, you provided the following information:

a) Technical Data Sheets on (b)(4)
b) Drug Master File Access Letter for (b)(4)
c) Statement of Compliance to California's Proposition 65
d) Compliance to CONEG Model Legislation
e) (b)(4) Assay for cytotoxicity

This information is not sufficient to establish the biocompatibility of the applicator for its use with Pre~Va lubricant. Although Item E demonstrates the non-cytotoxic effect of the applicator, Items A-D, while helpful in establishing the safety of the applicator in general, do not specifically address its sensitization or irritation potential. Therefore, additional biocompatibility testing should be conducted to address these issues.

As previously stated in our AI letter, we expect that biocompatibility testing will be conducted on the final version of the applicator after exposure to Pre~Va lubricant in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, in addition to the cytotoxicity testing already provided, sensitization and irritation tests should also be conducted. Per ISO 10993, sensitization testing should include either maximization or mouse local lymph node assay tests, and vaginal irritation testing should be completed to assess irritation. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

In lieu of testing, you may also consider contacting the applicator vendor and/or the applicator resin vendor to investigate if the applicator material is used to manufacture other products with a similar type and duration of patient contact. You will need to provide evidence that the material used for these other products is identical to that used for the proposed applicator and has a history of safe use.

3. Please note that if you do not provide sufficient testing or justification to the biocompatibility issues raised, you will be asked to remove the following statement from the indications for use, "Pre~Va may be deposited intravaginally using the applicator."

XVII. Contact History

The sponsor was contacted via telephone on April 14, 2008 regarding a missing certification letter from the applicator vendor stating applicator compliance to CONEG Model Legislation Regarding Heavy Metals. The sponsor provided a copy of the letter via e-mail on the same day.

XVIII. Recommendation

Additional Information Required.

Sharon Andrews
Reviewer

4/23/08
Date

Colin M Pollard
Branch Chief

4/23/08
Date

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Andrews, Sharon M

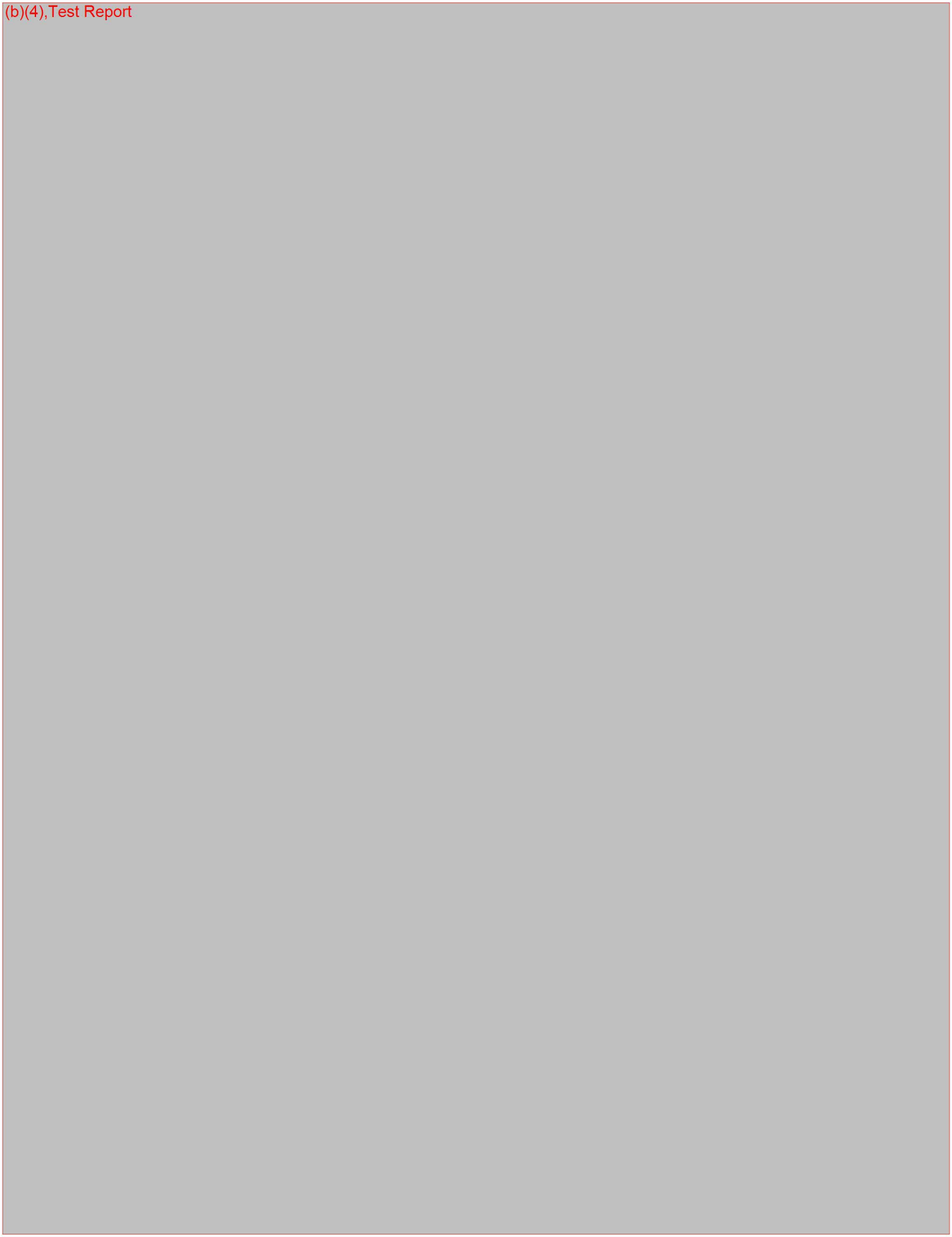
From: Dennis Clifton [dclifton@ingfertility.com]
Sent: Monday, April 14, 2008 4:03 PM
To: Andrews, Sharon M
Subject: Appendix C for K072741
Attachments: (b)(4) Compliance info Appendix C.pdf

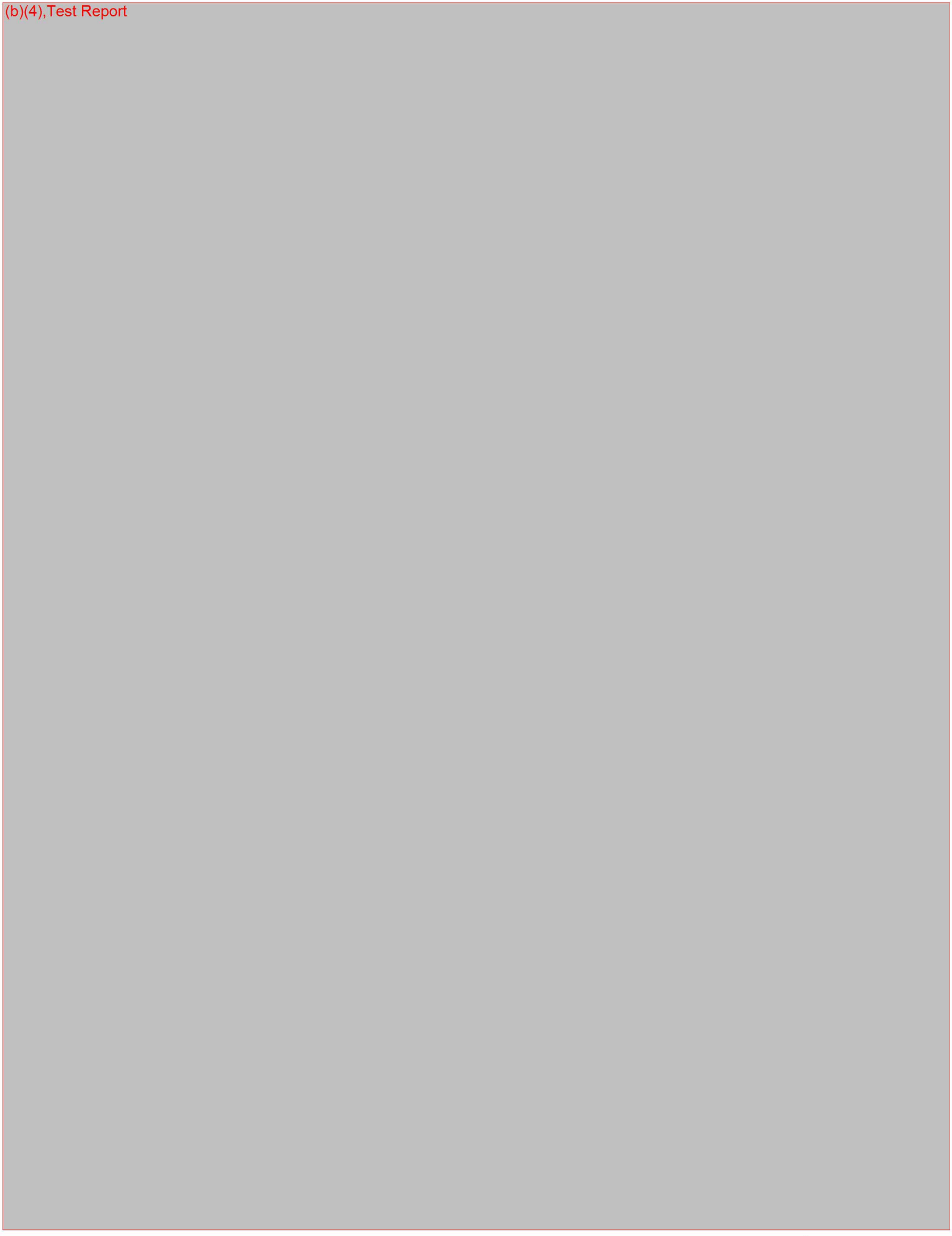
Hi Sharon,

Attached are the 3 letters for Appendix C. Sorry for the inconvenience. Please let me know if you need anything else.

Dennis

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149


(b)(4),Test Report


(b)(4),Test Report

(b)(4),Test Report

Food and Drug Administration
Office of Device Evaluation &
Office of In Vitro Diagnostics

COVER SHEET MEMORANDUM

From: Reviewer Name Sharon Andrews

Subject: 510(k) Number K072741

To: The Record

Please list CTS decision code A1

☐ Refused to accept (Note: this is considered the first review cycle, See Screening Checklist http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/ Screening Checklist)

☑ Hold (Additional Information or Telephone Hold).

☐ Final Decision (SE, SE with Limitations, NSE, Withdrawn, etc.).

Please complete the following for a final clearance decision (i.e., SE, SE with Limitations, etc.):		YES	NO
Indications for Use Page	*Attach IFU*		
510(k) Summary /510(k) Statement	*Attach Summary*		
Truthful and Accurate Statement.	*Must be present for a Final Decision*		
Is the device Class III? If yes, does firm include Class III Summary?	*Must be present for a Final Decision*		
Does firm reference standards? (If yes, please attach form from http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4136/ABBREVIATED STANDARDS DATA FORM.DOC)			
Is this a combination product? (Please specify category _____, see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_413b/COMBINATION%20PRODUCT%20ALGORITHM%20(REVISED%203-12-03).DOC			
Is this a reprocessed single use device? (Guidance for Industry and FDA Staff – MDUFMA - Validation Data in 510(k)s for Reprocessed Single-Use Medical Devices, http://www.fda.gov/cdrh/ode/guidance/1216.html)			
Is this device intended for pediatric use only?			
Is this a prescription device? (If both prescription & OTC, check both boxes.)			
Is clinical data necessary to support the review of this 510(k)?			
Does this device include an Animal Tissue Source?			
Is this device subject to Section 522 Postmarket Surveillance? (Postmarket Surveillance Guidance, http://www.fda.gov/cdrh/osb/guidance/316.html)	*Contact OSB.*		
Is this device subject to the Tracking Regulation? (Medical Device Tracking Guidance, http://www.fda.gov/cdrh/comp/guidance/169.html)	*Contact OC.*		

Regulation Number	Class*	Product Code
21 CFR 884.5300	II	NUC

(*If unclassified, see 510(k) Staff)

Additional Product Codes: _____

Review: Herbert Lerner (Acting) (Branch Chief) _____ (Branch Code) 12/4/07 (Date)

Final Review: _____ (Division Director) _____ (Date)

PRE-REVIEW FORM: COMPANY/DEVICE HISTORY

Please complete the pre-review form prior to beginning the review of this 510(k). This form is designed to be a tool to identify key items that may be important to consider regarding the regulation of the subject device and if you should even begin the review of the 510(k).

If you answer YES to questions 1, 2 or 3; do NOT begin the review of this 510(k):		**YES**	**NO**
1.	Are you aware of the submitter being the subject of an integrity investigation? (Please see H:\INTEGRITY LIST\CDRH REVIEWER SCREENING LIST.DOC)		
2.	Is the device exempt from 510(k) by regulation (Please see http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4134/510(K)%20EXEMPT%20%20FORM.DOC or subject to enforcement discretion (No regulation - See 510(k) Staff)?		
3.	Does this device type require a PMA by regulation? (Please see management.)		
Questions 4-8 are intended to help you start your review:		**YES**	**NO**
4.	Is this 510(k) a candidate for "Refuse to Accept"? (If so, please use the Traditional/Abbreviated or Special 510(k) Refuse to Accept Screening Checklist, http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4d69/Screening%20Checklist.doc)		
5.	a. Did the firm request expedited review? (See management,)		
	b. Was expedited review granted? (See *Guidance for Industry and FDA Staff: Expedited Review of Devices for Premarket Submissions*, http://www.fda.gov/cdrh/mdufma/guidance/108.html)		
6.	To the best of your knowledge, was there a pre-IDE, 513(g) or other pre-submission for this type of device?	Please list document number and/or date, here:	
7.	To the best of your knowledge, has a 510(k) previously been submitted for this specific device (i.e., previously found NSE or withdrawn)?	Please list document number, here:	
8.	Does this device have indications or technology that are cross-cutting and impact the review policy of another branch(es)? (Please contact other branch(es) and see *Guidance for Industry and FDA Staff on Bundling Multiple Devices or Multiple Indications in a Single Submission* http://www.fda.gov/cdrh/mdufma/guidance/1215.html)		

DEPARTMENT OF HEALTH AND HUMAN SERVICES MEMORANDUM

Food and Drug Administration
Office of Device Evaluation
9200 Corporate Boulevard
Rockville, MD 20850

Premarket Notification [510(k)] Review
Traditional/Abbreviated

K072741

Date: December 18, 2007
To: The Record
From: Sharon Andrews, Biomedical Engineer

Office: ODGB
Division: DRARD

510(k) Holder: INGfertility, LLC
Device Name: Pre~Va Vaginal Lubricant
Contact: Dennis Clifton, Pharm.D., Vice President
Address: 17206 South Spangle Creek Road, Valleyford, WA 99036
Phone: 509-443-0149
Fax: 509-471-9638
Email: dclifton@ingfertility.com

I. Purpose and Submission Summary

The 510(k) holder would like to introduce the Pre~Va vaginal lubricant into interstate commerce.

II. Administrative Requirements

	Yes	No	N/A
Indications for Use page (Indicate if: Prescription or **OTC**)	X		
Truthful and Accuracy Statement	X		
510(k) Summary or 510(k) Statement	X		
Standards Form			X

III. Device Description

	Yes	No	N/A
Is the device life-supporting or life sustaining?		X	
Is the device an implant (implanted longer than 30 days)?		X	
Does the device design use software?		X	
Is the device sterile?		X	
Is the device reusable (not reprocessed single use)?		X	
Are "cleaning" instructions included for the end user?			X

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IV. Indications for Use

Pre~Va vaginal lubricant is intended to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. *Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of a medical device.* As a personal lubricant, Pre~Va supplements the body's own natural lubrication fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. *Pre~Va is safe for use by couples trying to conceive* and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

The predicate device for the subject lubricant is the Pre' vaginal lubricant. Pre' vaginal lubricant is intended to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. As a personal lubricant, Pre' supplements the body's own natural lubrication fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre' may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

Pre' vaginal lubricant was cleared under 510(k) K051436 on October 13, 2006. It is classified as a condom under 21 CFR 884.5300 and procode NUC.

The intended use of the subject and predicate lubricants is not the same. The subject lubricant has an expanded indication, which is italicized above. However, the difference in the intended use does not alter the intended therapeutic or diagnostic effect.

The sponsor will be asked to rephrase the indications for use statement to clarify that it is used to lubricate specifically medical devices used in fertility interventions. The indications for use statement as it reads now states that Pre~Va can be used to lubricate any medical device.

V. Predicate Device Comparison

The Pre~Va and Pre' Vaginal lubricants have the exact same formulation. The ingredients their respective weight percent in the formulation and CAS Numbers are listed in the table below.

Ingredient	Weight Percent (%w/w)	CAS Number
Water	(b)(4)	7732-18-5
Hydroxyethylcellulose, NF		9004-62-0
Pluronic 127, NF		9003-11-6
Sodium Chloride, USP		7647-14-5
Arabinogalactan		9036-66-2
Sodium Phosphate		(b)(4)
Carbopol 934P, NF		9003-01-4
Methylparaben, USP		99-76-3
Sodium Hydroxide, NF		1310-73-2
Potassium Phosphate		(b)(4)

In addition, the specifications for the subject lubricant are the same as those of the predicate device.

These specifications are listed in the following table.

Physical Specifications/Tests	Ranges/Specifications
pH @ 25°C	7.20 – 7.45
Osmolarity	260 and 360 mOsmo/kg
Apparent Viscosity	8,500 – 12,000 cps
Specific Gravity	1.0 – 1.05
Microbial limits at 48 hours	0 cfu/ml pathogens; <100 cfu/ml other organisms
Endotoxin by LAL methodology	<0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA to > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility following 30 minute incubation with 10% diluted lubricant solution equals >80% of sperm in control medium

There are two primary differences between the predicate and subject lubricants: (1) the subject lubricant claims to safe to use by couples trying to conceive, and (2) the subject lubricant is packaged with a (b)(4) applicator. The consequences of these changes are discussed in the appropriate sections of this review memo.

The sponsor provided three samples of the applicator with the submission. The applicator has a (b)(4) (b)(4) and is made of (b)(4). The resin utilized for the applicator is in accordance with 21 CFR 177.1520, which describes "substances for use as basic components of single and repeated use food contact surfaces." This regulation is not applicable to the applicator for use with a lubricant.

The applicators are manufactured by (b)(4). The sponsor has provided engineering drawings noting the dimensions for the applicator. The fully extended length of the applicator is 8.9 inches, and the fully compressed length of the applicator is 4.9 inches. The diameter of the (b)(4) (b)(4)

The applicator can be (b)(4) and the lubricant can be squeezed into the applicator to a desired amount. The applicator is disposable.

VI. Labeling

Labeling has been provided which includes instructions for use and an appropriate prescription statement as required by CFR 21.807.87 (e). This product will be sold over the counter.

The sponsor has provided draft labeling that will be found on the lubricant package, the lubricant tube, and a draft package insert.

The package labeling (p.36) contains the following information: product claims, directions for use (personal and clinical), ingredients, warnings, caution statements, storage information, expiration date, and lot number.

The package labeling (email dated 11/28/07) contains the following information: product claims, directions for use (personal and clinical), ingredients, warnings, caution statements, expiration date, and lot number. The sponsor will be asked to place the storage information on the lubricant tube labeling.

The package insert (p.39) contains more detailed instructions for use, warnings, caution statements, storage information, ingredients, products specifications, and validated instructions for sterilization.

The principal display front of the package labeling contains the following statement, "Clinically Tested and Doctor Recommend." The sponsor has not provided any data in this submission to substantiate this claim. The sponsor will be asked to justify this claim. In addition, if the sponsor sufficiently justifies this claim, they will be asked to change this statement to "Clinically Tested and Doctor Recommended."

In the submission, the applicator is described as disposable; however in the instructions for use on the package labeling, lubricant tube, and the package insert, there is no mention of how to dispose of the lubricant. The sponsor will be asked to add the following statement at the end of the instructions for use, "The applicator is single use only. Dispose applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."

VII. Sterilization/Shelf Life/Reuse

Pre~Va vaginal lubricant is supplied non-sterile. It is specified to have microbial limits at 48 hours of 0 cfu/ml pathogens and <100 cfu/ml other organisms. The endotoxin limit is <0.5 EU/ml. These are identical to the specifications of the predicate lubricant.

The clinical instructions for use found in the package insert provide instructions for sterilization to a SAL of (b)(4) This is for when clinics desire a sterilized product for procedures such as intrauterine insemination and embryo transfer. These instructions are identical to those supplied with the predicate lubricant.

Stability testing was conducted (b)(4)
(b)(4)
Samples were found to be within range for all intervals tested (b)(4)

Physical Specification	Acceptable Range
(b)(4)	(b)(4)

The stability data was used to establish a shelf-life of (b)(4) for the predicate lubricant. (b)(4)
(b)(4)

The sponsor has not provided any information concerning the sterilization, packaging, or shelf-life of the applicator. The sponsor will be asked to provide this information.

VIII. Biocompatibility

This device is a surface device that is in contact with both the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation or intracutaneous activity tests must be completed.

The following biocompatibility testing was conducted on (b)(4) : rabbit vaginal irritation studies, rabbit penile irritation studies, human skin sensitization studies, and slug mucosal irritation test. The (b)(4) lubricant did not induce any irritation or sensitization reactions in the animals or human subjects. (b)(4)
results of biocompatibility testing (b)(4) are acceptable for the Pre~Va lubricant.

The sponsor has not provided any data supporting the biocompatibility of the applicator. The sponsor will be asked to provide this data.

IX. Software

This section does not apply to this submission.

X. Electromagnetic Compatibility and Electrical, Mechanical and Thermal Safety

This section does not apply to this submission.

XI. Performance Testing – Bench

Lubricant/Applicator Compatibility

The sponsor has not provided any testing evaluating the compatibility of the lubricant and the applicator. The sponsor will be asked to provide this information.

The following testing was conducted (b)(4)
(b)(4)

Condom Compatibility

Condom compatibility testing was conducted by (b)(4). Results from this testing indicated the predicate lubricant was compatible with both latex and polyurethane condoms and that the use of the lubricant had no statistically significant effects on tensile strength, elongation at break, or breaking force. Burst testing was not conducted. Testing was conducted on three brands of Latex condoms (Trojan, Durex, Lifestyles) and the (b)(4) polyurethane condom. The results of these tests are acceptable.

However, the sponsor will be asked to determine if Pre~Va vaginal lubricant remains condom compatible after exposure to the applicator.

Mouse Embryo Assay (MEA)

MEA is conducted to assess the potential toxicity of materials used in assisted reproduction devices to gametes and/or embryos. In order for a lubricant to be viewed as non-toxic, a minimum 86% of oocytes must develop normally.

The (b)(4) device was found to have no effect on the development of a 2 cell embryo at 24 hours to a blastocyst at 96 hours compared to a control. Ninety five percent of the embryos developed into blastocysts after exposure to the (b)(4) lubricant. The results of this test are acceptable.

Bovine In-Vitro Fertilization & Embryo Development (bIVF)

bIVF is used to evaluate the effect of lubricants on sperm prior to and during the fertilization process. For example, bIVF can show inferior embryo development resulting from fertilization by sperm that had damaged DNA, although fertilization itself was normal. Lubricants should cause no greater than a 15% drop of oocytes fertilized and development of blastocysts compared to the control medium.

There was not statistically significant difference between the (b)(4) lubricant and the control medium in terms of effect on fertilization or embryo development. Fertilization occurred at 77% frequency with the control medium, compared to 73% with the (b)(4) lubricant. Embryonic development occurred at 44% frequency, compared to 47% frequency with the (b)(4) lubricant. The results of this test are acceptable.

Sperm Motility Assay (Sperm/Lubricant Interaction Study)

The sperm motility assay was conducted to evaluate the direct effects of pure lubricant on sperm in semen. Sperm penetration and survival was assessed through visual observation.
Sperm was found to swim readily into and through the (b)(4) lubricant, and dissipate into it over time. In contrast, sperm did not penetrate through other leading lubricants, including FemGlide and KY Jelly. The results of this test are acceptable.

Sperm Chromatin Structure Assay

This study was conducted to evaluate sperm chromatin integrity following contact with a lubricant. Levels of DNA damage in sperm exposed to lubricant cultures should maintain 85% or more of the level of sperm DNA damage seen in control media without a lubricant.

The (b)(4) lubricant was found to not cause a significant decrease in chromatin integrity compared to the control. The control media had a percent DNA fragmentation index (%DFI) of 14.8%, while the (b)(4) lubricant had a %DFI of 15.5%. The results of this test are acceptable.

In-Vitro Fertilization & Embryo Development

This test was conducted at the request of the FDA (b)(4) to evaluate the effects of undiluted lubricant on sperm samples ability to penetrate and fertilize an oocyte, with continued follow-up to assess embryo development.

Sperm exposed (b)(4) were found to have no significant difference from the control sperm (no exposure to lubricant) in their ability to fertilize oocytes or support embryonic development. The results of this test are acceptable.

The above described tests adequately show that the subject lubricant is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process. The evaluation of these tests was conducted using, "General comments on Docket No. 2003N-0539, OTC Designation for Vaginal Lubricants, Need for improved labeling for use of vaginal lubricants by trying-to-conceive couples." This document was written by JE Ellington and GD Clifton and was provided by Dr. Michael Bailey, OGDB Biologist, for determination of the type of testing needed for the indicated use of Pre~Va vaginal lubricant and the evaluation of this testing.

The sponsor has not provided the results of two tests listed in the document, including computer aided sperm analysis for quantitative assessment of sperm motility and cervical mucosal testing. Cervical mucosal testing is needed to determine the ability of sperm to penetrate the cervical mucous membrane following lubricant exposure. This testing may be completed as either a post coital test in human subjects or in an appropriate animal model. The sponsor will be asked to justify why they have not conducted this testing.

XII. Performance Testing – Animal

This section does not apply to this submission.

XIII. Performance Testing – Clinical

This section does not apply to this submission.

XIV. Substantial Equivalence Discussion

	Yes	No	
1. Same Indication Statement?		X	If **YES** = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?		X	If **YES** = Stop **NSE**
3. Same Technological Characteristics?	X		If **YES** = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If **YES** = Go To 6
5. Descriptive Characteristics Precise Enough?		X	If **NO** = Go To 8 If **YES** = Stop **SE**
6. New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NSE**
7. Accepted Scientific Methods Exist?			If **NO** = Stop **NSE**
8. Performance Data Available?		X	If **NO** = Request Data
9. Data Demonstrate Equivalence?			Final Decision:

Note: See http://eroom.fda.gov/eRoomReg/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4148/FLOWCHART%20DECISION%20TREE%20.DOC for Flowchart to assist in decision-making process. Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

1. Explain how the new indication differs from the predicate device's indication:

   The new indication states that Pre~Va vaginal lubricant is safe to use for couples who are trying to conceive and may be deposited intravaginally using an applicator.

2. Explain why there is or is not a new effect or safety or effectiveness issue:

   The safety and effectiveness issues raised have been previously addressed with fertility treatments and vaginal applicators.

3. Describe the new technological characteristics:

4. Explain how new characteristics could or could not affect safety or effectiveness:

5. Explain how descriptive characteristics are not precise enough:

   Descriptive characteristics are not precise enough to evaluate lubricant-applicator compatibility or the safety of the lubricant for use by couples who are trying to conceive.

6. Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:

7. Explain why existing scientific methods can not be used:

8. Explain what performance data is needed:

Performance data is needed to evaluate lubricant-applicator compatibility and the safety of the lubricant for couples who are trying to conceive.

9. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

XV. Deficiencies

Indications for Use

1. Please note that if you do not provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies, you will be asked to remove the following statement(s) from the indications for use, "Pre~Va is safe for use by couples trying to conceive," and/or "Pre~Va may be deposited intravaginally using the applicator."

2. Your indications for use statement contains the following statement, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of a medical device." Please rephrase this statement to read as follows, "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions." Your indications for use page and 510(k) summary page should be updated accordingly.

   Please note that as state previously, this change will only be necessary if you provide sufficient testing or justification regarding the issues raised in the bench testing deficiencies.

Labeling

3. The principle display front of the package labeling contains the following statement, "Clinically Tested and Doctor Recommend." However, you have not provided any data in this submission to support this claim. Please provide data to sufficiently justify this claim, or please remove this claim from the labeling.

   In addition, if you sufficiently justify this claim, please rephrase this claim to read as follows, "Clinically Tested and Doctor Recommended."

4. In your submission, the applicator is described as disposable; however, the instructions for use contain do not describe how to dispose of the applicator after use. In order to avoid reuse of the applicator, please add the following statement to the end of the instructions for use on the package labeling, lubricant tube, and the package insert, "The applicator is single use only. Dispose applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."

5. Please place the storage conditions for the Pre~Va vaginal lubricant on the lubricant tube labeling.

Sterilization/Packaging/Shelf-Life

6. You have not provided any information in this submission regarding the sterilization, packaging, or shelf-life of the applicator. Please provide the following information regarding the applicator.

   a. Describe the method and procedure of sterilization. If the applicator is not provided sterile, justify why sterilization is not necessary for the device as it is intended to be used.
   b. Describe how the applicator will be packaged. If the applicator is provided sterile, describe how the packaging maintains device sterility.
   c. Provide a shelf-life for the applicator, and describe in detail how this shelf-life was determined. (b)(4)

(b)(4)

Biocompatibility

7. You state in your submission that the resin utilized for the applicator is in accordance with 21 CFR 177.1520. This regulation describes "substances for use as basic components of single and repeated use food contact surfaces," and therefore, it does not apply to the applicator as it is intended to be used with the Pre~Va vaginal lubricant.

   As a result, you have not provided sufficient information in this submission regarding the biocompatibility of the applicator. Please provide the complete test protocols, results, and conclusions of this testing.

   We expect that biocompatibility testing will be conducted on the final, sterilized version of the device in accordance with ISO 10993-1: Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing. The applicator is considered a surface device that contacts the skin and mucosal membranes for a limited (<24 hour) contact duration. Therefore, cytotoxicity, sensitization, and irritation tests should be conducted. Please note that polar and non-polar extracts should be used for sensitization and irritation studies.

   If you believe that biocompatibility testing is not necessary for clearance of this device, please provide justification for your decision. Please note that if your justification is not sufficient, you will be asked to conduct biocompatibility testing.

Bench Testing

8. In this submission, you state that Pre~Va will be supplied with an applicator that may be used to deposit the lubricant intravaginally. However, you have not provided any information to assess the compatibility of the applicator with the lubricant. This information is needed to ascertain if any unfavorable interactions may occur between the applicator and the lubricant that will affect the safety of this device for use by couples who are trying to conceive. Please determine if Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator. Your determination of compatibility should take into account both the duration and the environmental conditions (i.e. temperature) of lubricant exposure to the applicator during both normal and exaggerated use conditions.

   Please note that if you are unable to show that Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator, you will not be able to market the applicator for use with the lubricant.

9. Please also determine if Pre~Va remains compatible with both latex and polyurethane condoms after contact with the applicator.

   Please note that if you are unable to show that Pre~Va is compatible with both latex and polyurethane condoms after contact with the applicator, you will not be able to market the applicator for use with the lubricant, or you will have to remove the claim of "compatible with latex and polyurethane condoms" from the product labeling.

10. You have qualitatively assessed sperm motility after contact with Pre~Va vaginal lubricant and sperm penetration through Pre~Va via visual observation. However, you have not provided a quantitative assessment of sperm motility, which is necessary to objectively determine the effect of Pre~Va vaginal lubricant on sperm motility and velocity parameters. Please provide the complete test protocols, results, and conclusions from this testing.

If you believe that quantitative analysis of sperm motility is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient, you will be asked to conduct qualitative sperm analysis.

11. You have not provided the results of cervical mucosal penetration testing for the Pre~Va vaginal lubricant. The results of this testing is necessary to determine that the use of Pre~Va vaginal lubricant has no detrimental effect on sperm penetration into the cervical mucous membrane. This testing may be done as either a post-coital test in human subjects or in an animal cervical mucosal model. If you choose to conduct testing on an animal model, please justify the use of the animal model that you select.

    If you believe that cervical mucosal testing is not necessary for clearance of this device, please justify your decision. Please note that if your justification is not sufficient you will be asked to complete cervical mucosal testing.

XVI. Contact History

The sponsor was sent an e-mail on November 27, 2007 asking for additonal information regarding the applicator. The sponsor responded the same day with applicator specifications, engineering diagrams, and a photo of the applicator.

The sponsor was sent an e-mail on November 28, 2007 asking for a sample of the applicator to be sent and requesting draft labeling for the lubricant tube. The sponsor responded the same day with a copy of the draft labeling. A sample of the correct applicator was received on November 29, 2007. A sample of the lubricant was also sent with the applicator sample.

XVII. Recommendation

Request for Additional Information.

Sharon Andrews
Reviewer

12/20/07
Date

Branch Chief

Date

Andrews, Sharon M

From: Dennis Clifton [dclifton@ingfertility.com]
Sent: Wednesday, November 28, 2007 3:14 PM
To: Andrews, Sharon M
Subject: RE: K072741 - Pre~Va Vaginal Lubricant
Attachments: Proposed Tube Labeling.doc

Dear Ms. Andrews,

Attached is the draft labeling for the tube. I apologize for the oversight in not including this with the original application.

With regard to the applicator; I have sent one to you via UPS overnight. If you do not receive it by tomorrow afternoon please let me know.

Sincerely,

Dennis

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

From: Andrews, Sharon M [mailto:sharon.andrews@fda.hhs.gov]
Sent: Wednesday, November 28, 2007 10:02 AM
To: Dennis Clifton
Subject: RE: K072741 - Pre~Va Vaginal Lubricant

Dear Dr. Clifton,

Thank you for your prompt response.

The sample applicators provided with the submission (b)(4) Could you please send me a sample of the applicator (b)(4) The sample can be sent directly to me at the address below.

I have an additional question regarding the labeling/packaging of the lubricant. You have provided a copy of the draft labeling for both the lubricant package (principle display front and principle display panel back and sides) and the package insert. Will there be labeling on the lubricant tube itself? If yes, please provide a draft copy of this labeling.

Please note that additional deficiencies may be identified as I continue my review of this file.

Thank you.

Sincerely,

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB
9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850
Phone: 240-276-4148
Fax: 240-276-4156
sharon.andrews@fda.hhs.gov

From: Dennis Clifton [mailto:dclifton@ingfertility.com]
Sent: Tuesday, November 27, 2007 3:53 PM
To: Andrews, Sharon M
Subject: FW: K072741 - Pre~Va Vaginal Lubricant

Dear Ms. Andrews,

Please see my answers below in response to each of your questions. As indicated under question 1. I have attached the specifications of the applicator as provided to us by the supplier.

Please contact me if I may be of any further assistance with your review.

Sincerely,

Dennis

Dennis Clifton, PharmD
Vice President
INGfertility
509-443-0149

From: Andrews, Sharon M [mailto:sharon.andrews@fda.hhs.gov]
Sent: Tuesday, November 27, 2007 12:13 PM
To: dclifton@ingfertility.com
Subject: K072741 - Pre~Va Vaginal Lubricant

Dear Dr. Clifton,

My name is Sharon Andrews, and I am the lead reviewer for your 510(k) submission K072741 regarding the Pre~Va Vaginal Lubricant. I have a few questions regarding the applicator that may be used with this lubricant.

(1) You state that the lubricant (b)(4)

samples of the applicator you have provided with the submission? The sample applicators we sent were from the applicator manufacturer to confirm the size and fit on the tube. (b)(4) (b)(4) I apologize for any confusion this may have caused. A copy of the exact applicator specifications (b)(4) (b)(4). I have also enclosed a scanned (b)(4) that we have in house. I can forward the applicator itself to you for inclusion in the submission if desired.

(2) Will the applicator (b)(4)

(b)(4)

(2) How much lubricant (b)(4)

(b)(4)

(3) How much lubricant (b)(4)
(b)(4)

Please respond to these questions as soon as possible, preferably by the end of this week, Friday, November 30th, so that I can proceed with the review of this file.

Please note that additional deficiencies may be identified as I continue the review of this file.

Thank you.

Sincerely,

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB
9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850
Phone: 240-276-4148
Fax: 240-276-4156
sharon.andrews@fda.hhs.gov

(b)(4),drawings,Product Specifications

(b)(4),drawings,Product Specifications

(b)(4),drawings,Product Specifications

(b)(4),drawings,Product Specifications

(b)(4),drawings,Product Specifications

PROPOSED TUBE LABELING
PRE~VA VAGINAL LUBRICANT

PRINCIPAL DISPLAY FRONT
Logo
Pre~Va™ Vaginal Lubricant
"Fertility~Friendly*"

- pH Balanced to Fertile Cervical Mucus
- *Uniquely Developed to Not Harm Sperm
- Applicator Coats Vagina with Moisture

Net Wt. 40 gm tube

Pre~Va provides moisture without harming sperm. For use any time, even while trying to conceive. Learn more & view *clinical studies at www.pre-va.com.

PRINCIPAL DISPLAY BACK & SIDES

DIRECTIONS: See enclosed insert
USES: Pre~Va Lubricant supplements natural lubricating fluids to enhance the ease and comfort of intimate sexual activity. Pre~Va is also used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions.

INGREDIENTS: Purified Water, Hydroxyethylcellulose, Pluronic 127, Sodium Chloride, Sodium Phosphate, Carbopol 934, Arabinogalactan, Methylparaben, Sodium Hydroxide, Potassium Phosphate

IMPORTANT: Store at room temperature. If the seal on the tube is damaged or opened, DO NOT USE, and return entire contents to place of purchase.
CAUTION: If irritation occurs discontinue use immediately, and if it persists consult a physician.

QUESTIONS: 888.471.7333 or 509.443.0149.
Manufactured in the USA for INGfertility, Valleyford, WA
US Patent #6,593,309 B2

CRIMP OF TUBE:
Expiration Date
Lot #

INGfertility

"Naturally Enhancing Reproduction"™

November 28, 2007

Sharon M. Andrews
Biomedical Engineer, FDA/CDRH/OGDB
9200 Corporate Boulevard (HFZ - 470)
Rockville, MD 20850

RE: K072741 - Pre~Va Vaginal Lubricant

Dear Ms. Andrews:

Per your request, enclosed please find a sample applicator for the Pre~Va Vaginal Lubricant. This applicator has the fill lines marked on it. I have also enclosed a sample of the product in the tube for your review and testing with the applicator.

Please let me how we may further assist you in your review of our submission.

Sincerely,

Dennis Clifton, PharmD
Vice President

The Makers of *Pre-Seed* ® *"Fertility-Friendly" Intimate Moisturizer*

17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

INGfertility

K072741/S1

March 18, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

FDA CDRH DMC

MAR 20 2008

Received

RE: K072741
Pre~Va Vaginal Lubricant

Dear Sir/Madam:

Enclosed with this letter please find the information requested as per your letter of December 21, 2007 with regards to the above referenced 510(k) premarket notification.

We appreciate the insightful comments and questions received from the Reviewer. Every attempt has been made to provide the information requested along with supplemental material as necessary.

The enclosed binders contain the information requested. The primary response and selected appendices are also provided in electronic form on the enclosed CD. In addition, we have included copies of referenced articles in the response. These copies are bound in alphabetical order.

We believe that the reviewer may also benefit by knowing the biography of the INGfertility CEO, Joanna Ellington, PhD. Dr Ellington is also co-author of the 510(k) submission. Her biography is attached.

Thank you in advance for the further review of our application. If you have questions regarding the content of the information provided please contact me at (509) 443-0149 or email dclifton@ingfertility.com.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

K48

17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.473.9638
www.ingfertility.com

INGfertility

March 25, 2008

Food and Drug Administration
Center for Devices and Radiological Health
Attn: Janee Sims
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

RE: K072741 Supplement 1 – electronic copy
Pre~Va Vaginal Lubricant

Dear Ms. Sims:

Enclosed with this letter please find the electronic copy of the paper response for the above referenced document mailed to CDRH on March 18, 2008. The enclosed CD is to replace the one submitted with the paper response. Please note that the information contained on the CD is an exact duplicate of that submitted in paper form on March 18, 2008.

If you have any information regarding this matter please contact me at (509) 443-0149 or email dclifton@ingfertility.com.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

K2

17206 Spangle Creek Road
Valleyford, Washington 99036
Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

March 18, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

RE: K072741
Pre~Va Vaginal Lubricant

Dear Sir/Madam:

Enclosed with this letter please find the information requested as per your letter of December 21, 2007 with regards to the above referenced 510(k) premarket notification.

We appreciate the insightful comments and questions received from the Reviewer. Every attempt has been made to provide the information requested along with supplemental material as necessary.

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Thank you in advance for the further review of our application. If you have questions regarding the content of the information provided please contact me at (509) 443-0149 or email dclifton@ingfertility.com.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

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Pre~Va Vaginal Lubricant
510(k) Application No. K072741

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* Sections 1-8 correspond to December 21, 2007 correspondence from Dr. Pollard

Bench Testing

1. Compatibility testing of applicator with the lubricant.

The reviewer requested that INGfertility provide information demonstrating that interaction of the lubricant with the applicator does not affect the safety of this device (lubricant) for use by couples who are trying to conceive.

In the following, INGfertility has demonstrated, using historical (Sections A and B) and new data (Section C), that interactions between the (b)(4) applicators and the lubricant do not affect the safety of the device.

A. The safety of the (b)(4) applicator to be marketed with Pre~Va lubricant is supported by information gathered from our vendor (b)(4) (b)(4). The following information can be found in the referenced appendices.
   - ***I.*** Technical data sheets on the resin – (b)(4) ***(Appendix A)***
   - ***II.*** A DMF access letter for the (b)(4) resin from (b)(4) ***(Appendix B)***
   - ***III.*** Statement of compliance to California's Proposition 65 ***(Appendix C)***
   - ***IV.*** Certification by vendor stating compliance meeting requirements of the Food and Drug Administration 21 CFR, 177.1520 for articles or components intended for use in contact with food. ***(Appendix C)***
   - **V.** Compliance to CONEG Model Legislation regarding heavy metals. ***(Appendix C)***

   For purposes of this section please specifically note item (III.). The statement of compliance to California's Proposition 65 specifically states that (b)(4) does not require a warning statement" as it does not contain chemical substances which are "known to the State [California] to cause cancer or reproductive toxicity".

B. Previous compatibility testing of Pre~Va Vaginal lubricant with (b)(4) containers.
   - **I.** The vast majority of safety and biocompatibility testing conducted with Pre~Va and its predicate were performed following storage of the lubricant gel in (b)(4)
   - **II.** The specification sheet and certifications for the (b)(4) (b)(4) in these storage containers are provided in ***Appendix D***. Although the resin used in these is somewhat different from that in the proposed applicator, it is highly unlikely these differences would result in any impact on the compatibility with the lubricant during the short time of interaction required for lubricant application.

III. The following assays, demonstrate that Pre~Va does not impair sperm function or embryo development, after storage of the lubricant in closed (b)(4) resin containers as specified above. The details of each study can be found in the (b)(4) (b)(4) supplied with the initial submission.

- Effects on Fertilization and Embryo Development
  - Mouse Embryo Assay (b)(4) ***Section 3, Fertility Interventions – and - Section 3 Appendix G)***
  - Bovine in vitro fertilization and embryo development (b)(4) ***Section 3, Fertility Interventions – and - Section 3 Appendix H – and – Section 5, Appendix E)***
- Sperm Motility (b)(4) ***, Section 3, Fertility Interventions –and- Section 3 Appendix I)***
- Sperm/Lubricant Interactions (b)(4) ***, Section 3, Fertility Interventions –and- Section 3 Appendix J)***
- Effects on Sperm Chromatin (b)(4) ***, Section 3, Fertility Interventions –and- Section 3 Appendix K)***

IV. Long-term stability testing of lubricant samples stored in closed (b)(4) containers has demonstrated that there is no effect of these (b)(4) containers on the physical properties or gamete /embryo safety profile during storage.

- Please refer to the (b)(4) (b)(4) ***Section 3, Shelf Life)*** for the detailed protocol and results for stability testing.

C. Additional studies, as requested, have been conducted to further support that "Pre~Va is non-toxic to sperm, oocytes, and developing embryos and does not interfere with the fertilization process after contact with the applicator". Methods, raw data, and results of the completed studies can be viewed in the referenced Appendices.

I. Sperm Motility ***(Appendix E)***
II. Mouse Embryo Assay ***(Appendix F)***
III. Bovine In Vitro Fertilization and Embryo Development ***(Appendix G)***
IV. Bovine Cervical Mucus Penetration ***(Appendix H)***

All four of these studies compared lubricant not exposed to the intravaginal applicator to lubricant exposed to either: a) the applicator for (b)(4) or b) the applicator (b)(4) With typical personal use, the lubricant will be exposed to the applicator for (b)(4) . Therefore the exposure times chosen represent, broadly, typical and extreme use conditions. We did not believe it necessary to conduct these studies at varying temperatures as (b)(4) (b)(4)

(b)(4)

Unless otherwise noted, the concentration of Pre~Va in each assay was at (b)(4) as previously justified (b)(4) (b)(4).

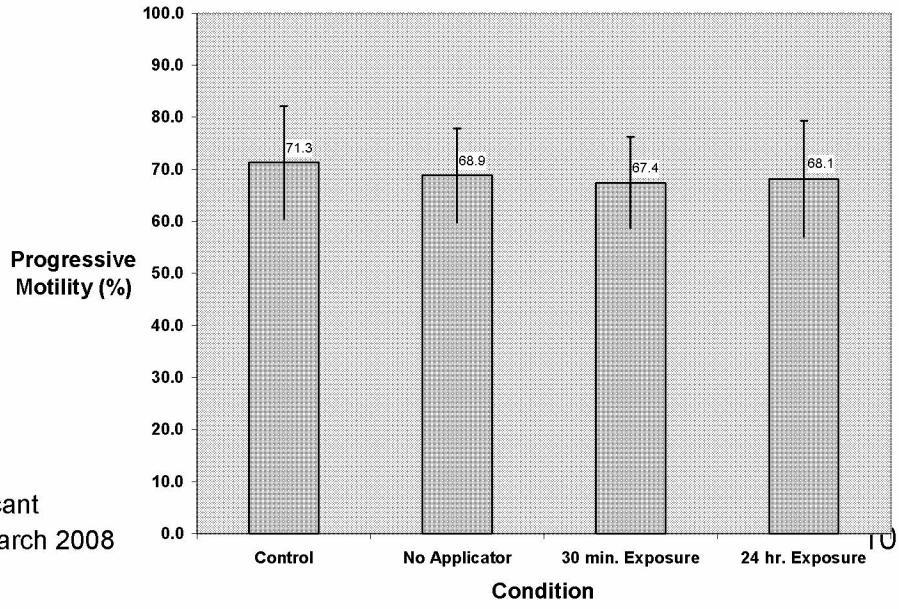
I. Sperm Motility

In this study we determined whether or not short-term exposure of Pre~Va lubricant, to the intravaginal applicator comprised of (b)(4) (b)(4) would alter the effects of the lubricant on human sperm motility. The methods for sperm motility analysis, results, and raw data from this study are provided in ***Appendix E***.

This study was conducted by (b)(4) (b)(4) (b)(4) Sperm motility was performed on (b)(4) semen collected from healthy male donors. Each sperm sample was (b)(4) (b)(4). Pre~Va, previously exposed to the applicator for 0 hrs (no exposure) (b)(4), was added respectively to (b)(4) aliquots, to achieve final concentrations of (b)(4) (b)(4) aliquot served as the control. Specimens were incubated for (b)(4) (b)(4)

Results from motility testing are summarized in Figure 1 below and demonstrate that exposure of the lubricant to the applicator for (b)(4) and (b)(4) does not alter the lubricant's effect on progressive sperm motility (b)(4)

Figure 1. Effect of Pre~Va on Human Sperm Motility Following Exposure to (b)(4) Resin



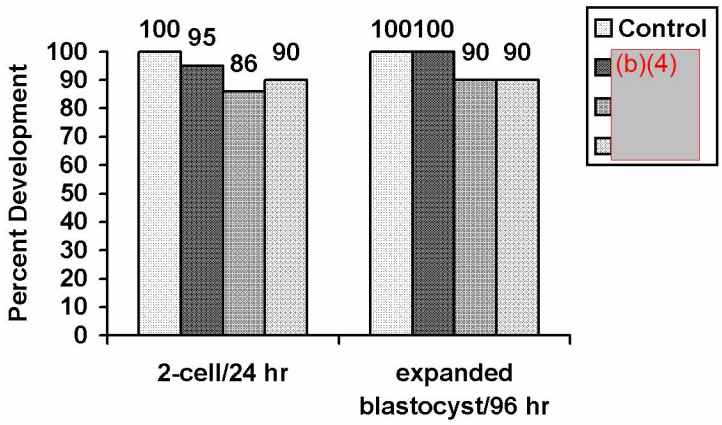
II. Mouse Embryo Assay

In this study we determined whether or not short-term exposure of Pre~Va lubricant to the intravaginal applicator comprised of (b)(4) Resin, would alter the effects of the lubricant on the Mouse Embryo Assay (MEA). The methods, Certificate of Analysis, and findings from this study are provided in ***Appendix F***.

This study was conducted by (b)(4) including completion of Special Control assays for fertility devices involving gamete contact.

For a device to be viewed as non-toxic in the MEA, a minimum ≥ 80% of 1-cell mouse embryos need to develop normally to the blastocyst stage. Results from MEA testing of lubricant exposed to the applicator are summarized in Figure 2 below. These data show that there was no difference in embryo development following incubation with a control (no lubricant), or Pre~Va with (b)(4) exposure to the intravaginal applicator. Contact with the applicator does not alter the lubricant's effect on embryo development, in this Special Control assay for gamete/embryo toxicity.

Figure 2. Effect of Pre~Va on the Mouse Embryo Assay Following Exposure to (b)(4) Applicators



III. Bovine In Vitro Fertilization and Embryo Development

In this study we determined whether or not short-term exposure of Pre~Va lubricant to the intravaginal applicator comprised of (b)(4) Resin, would alter the effects of the lubricant on the Bovine In-Vitro Fertilization (IVF) and Embryo Development Assay. The methods, raw data, and findings from this study are provided in ***Appendix G***.

This study was performed by (b)(4) (b)(4).

Results from this experiment are summarized in Figures 3 and 4 below, and demonstrate that under the experimental conditions tested:

1. Exposure of Pre~Va lubricant to applicators comprised of (b)(4) Resin does not alter ($p > 0.05$) the effect of the lubricant on in vitro fertilization of bovine embryos (Figure 3). Meaning specifically, that a similar percentage of oocytes were fertilized in vitro in: control medium (without lubricant), medium with (b)(4) lubricant added after (b)(4) storage time in the applicator, and medium with (b)(4) lubricant added after either (b)(4) hr storage time in the applicator.
2. Exposure of Pre~Va lubricant to applicators comprised of (b)(4) for (b)(4) does not alter ($p > 0.05$) the effects of the lubricant on the subsequent development of bovine embryos (Figure 4). Meaning specifically, that a similar percentage of the fertilized oocytes developed normally to blastocysts following exposure to: control medium (without lubricant), medium with (b)(4) lubricant added after (b)(4) storage time in the applicator, and medium with (b)(4) lubricant added after either (b)(4) hr storage time in the applicator. Although, the percent of developing embryos following exposure to the (b)(4) applicator stored lubricant, tended to be less than that found in the other treatments ($p=0.0827$).

Figure 3. Effect of Pre~Va on Fertilization Of Bovine Oocytes Following Exposure to (b)(4) Applicator

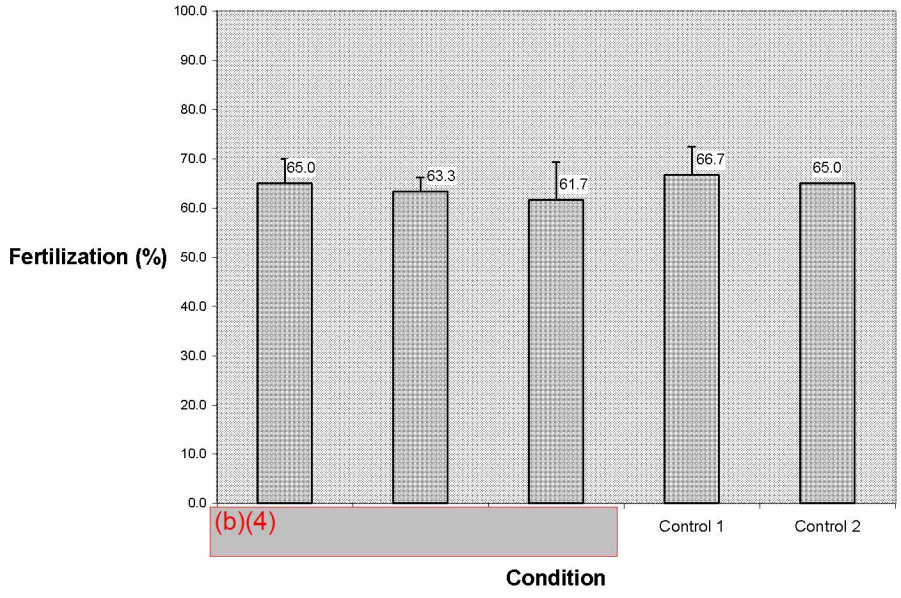
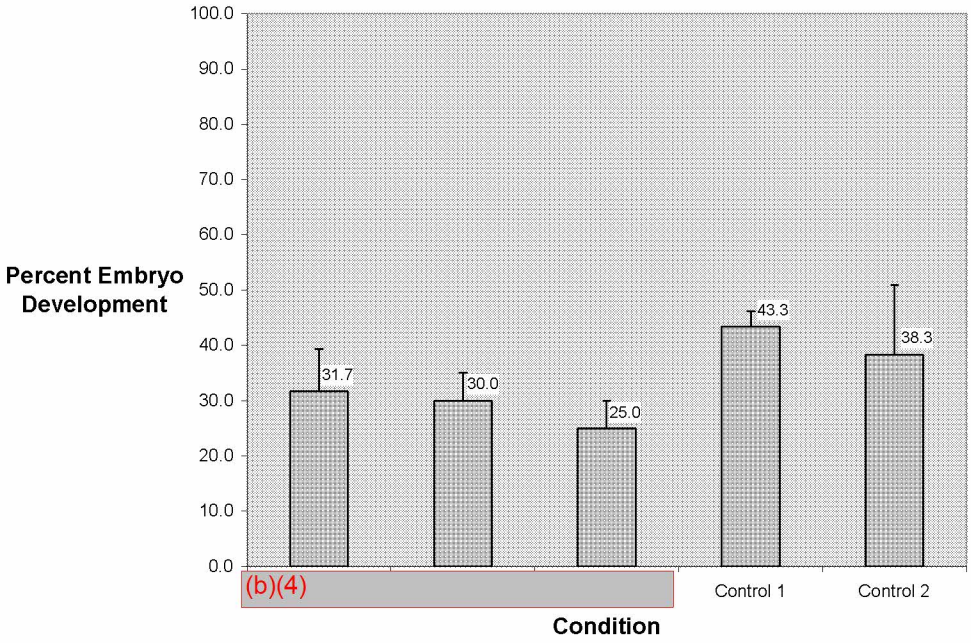


Figure 4. Effect of Pre~Va on Bovine Embryo Development Following Exposure to (b)(4) Applicator.



IV. Bovine Cervical Mucus Penetration

In this study we determined whether or not short-term exposure of Pre~Va lubricant to the intravaginal applicator comprised of (b)(4) (b)(4) would alter the effects of the lubricant on the Bovine Cervical Mucus Penetration Test (BCMPT). The rationale, methods, raw data, and findings from this study are provided in ***Appendix H***.

Briefly, penetration of cryopreserved bull sperm into columns of cow estrus cervical mucus was observed, following exposure to (b)(4) concentration of Pre~Va both with and without applicator exposure. Outcomes included vanguard sperm (furthest distance penetrated) and sperm density at two set distances of the mucus column after (b)(4) of incubation.

This study was performed by (b)(4) (b)(4).

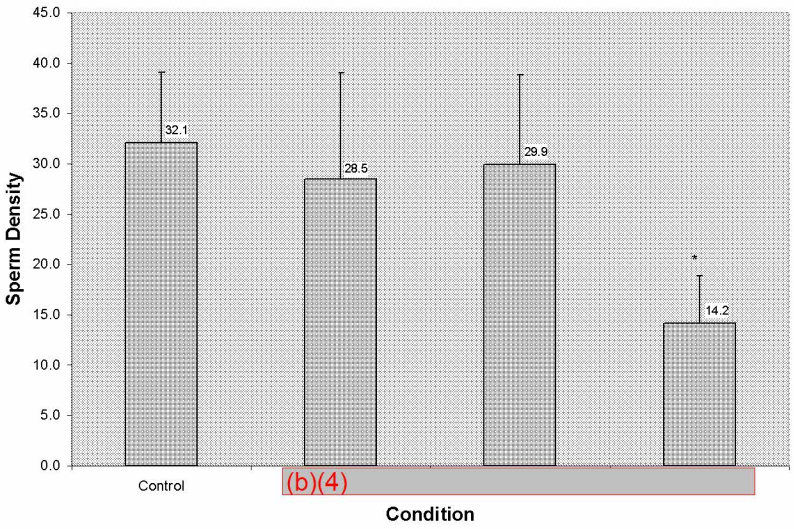
Please see the rationale for Bovine Cervical Mucus Penetration Test in Section 4 below; Cervical Mucosal Penetration Testing.

Results from this experiment are shown in Figures 5 and 6 and demonstrate that under the experimental conditions tested:

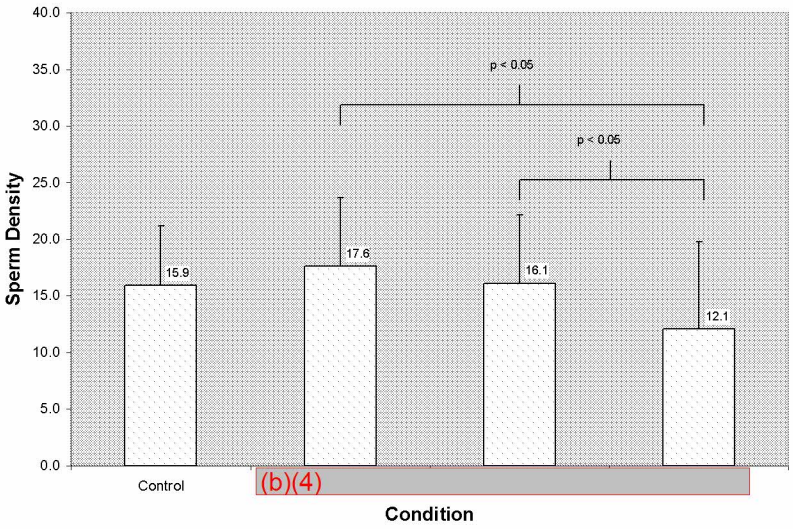
1. Exposure of Pre~Va lubricant to intravaginal applicators comprised of (b)(4) does not alter ($p > 0.05$) the effects of the lubricant on bovine cervical mucus penetration as measured by sperm density at set distances in a mucus column, or by vanguard sperm penetration (Figures 5 and 6) after (b)(4) of incubation.
2. In contrast, bovine cervical mucus penetration, as measured by sperm densities at (b)(4), was decreased ($p < 0.05$) when Pre~Va lubricant was stored in the (b)(4) applicator for (b)(4) (Figure 5).
3. Vangaurd penetration into sperm cervical mucus was also decreased ($p < 0.05$) following exposure of Pre~Va lubricant to applicators comprised of (b)(4) (Figure 6).

Figure 5. Effect Of Pre~Va on Sperm Density in Bovine Cervical Mucus Following Exposure to (b)(4) Intravaginal Applicator at: a) (b)(4) or b) (b)(4)

A. Density at (b)(4)

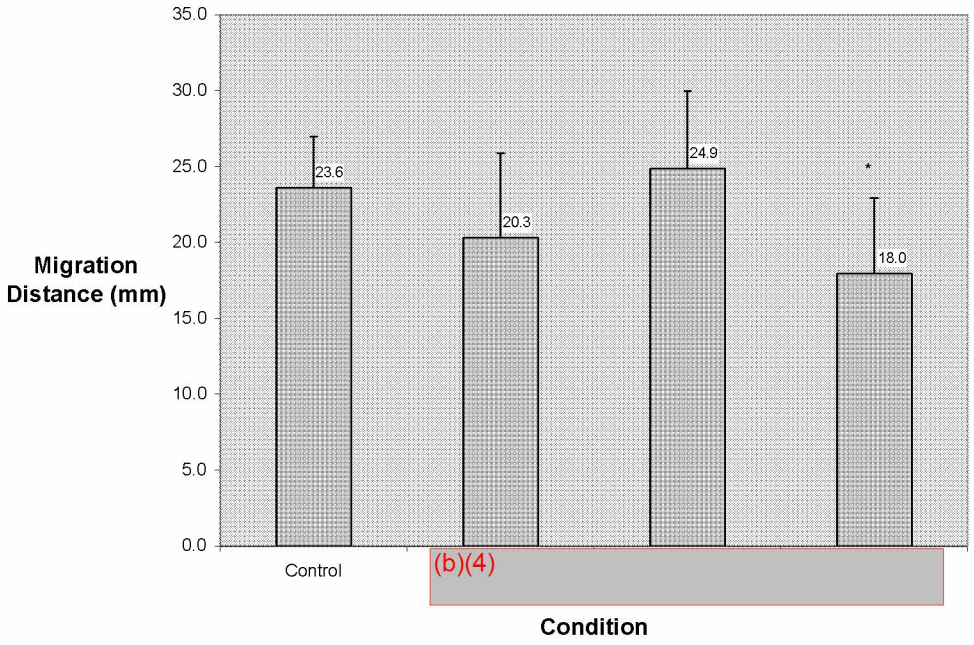


B. Density at (b)(4)



*$p < 0.001$ compared to other conditions.

Figure 6. Effect of Pre~Va on (b)(4) Vangaurd Sperm Bovine Cervical Mucus Penetration Following Exposure to (b)(4) (b)(4) Applicator (* p < 0.001 compared to other conditions)



D. Conclusions and Interpretation from Compatibility Testing of Applicator with the Lubricant.

Compatibility testing of the intravaginal applicator with Pre~Va vaginal lubricant demonstrated the following

I. The lubricant remains non-toxic to human sperm, bovine oocytes, and developing embryos (mouse and bovine) and does not interfere with the fertilization process (bovine in vitro model) after contact with the applicator for up to (b)(4).
II. The lubricant does not interfere with bovine cervical mucus penetration after contact with the applicator for up to (b)(4)
III. The lubricant remains non-toxic to human sperm, developing mouse embryos and does not interfere with fertilization after contact with the applicator for up to (b)(4).
IV. Following contact of the lubricant with the applicator for (b)(4), a reduction in overall cervical mucus penetration was observed, as well as, a tendency for decreased embryo development.

Because of the experimental design, it is not possible to determine if the observed reduction in cervical mucus penetration in the (b)(4) group was due to chemical interactions of the lubricant with the applicator, or if it was due to the effect of the lubricant being exposed to the atmosphere for (b)(4)

(b)(4)

E. Suggested Labeling Changes Based on Compatibility Testing Results

Despite the mechanism of the observed effect, and despite that a majority of the biocompatibility tests done were not effected, we propose that language should be added to the package insert recommending that the product be stored in the applicator no longer than 30 minutes prior to use. (b)(4) (b)(4) we are also adding language regarding closure of the tube following use.

The following language has been added to the "Personal Use" and "Clinic Use" Directions section of all labeling (See ***Appendix L***):

- **Do not store lubricant in applicator for more than 30 minutes prior to use.**
- **Keep cap tightly applied to Pre~Va tube between uses**

2. Condom Compatibility after Contact with the Applicator.

A. Requested Changes in Labeling/Instruction Regarding Condom Compatibility

The reviewer requested that INGfertility perform condom compatibility studies with the lubricant following exposure to the applicator in order to allow claims of compatibility with latex and polyurethane condoms. We believe that in addition to performing some additional compatibility studies, that this issue can be addressed by changes in the product labeling.

Lubrication of latex and polyurethane condoms is to be performed without use of the applicator (i.e. directly from the tube). The following changes to the Outer Package and Package Insert language are proposed to address this issue (new language is highlighted):

Change to outer carton Label/ Directions Section (See ***Appendix L***)

Personal Use:

Pre~Va's moisture can best mimic natural secretions, when applied intravaginally. Remove seal from tube opening before initial use. Remove applicator from pouch and twist firmly onto the tube for filling. Fill applicator with the desired amount of Pre~Va, to relieve

vaginal dryness. Insert applicator into vagina to deposit Pre~Va prior to intercourse. See enclosed insert for complete directions and information.

Pre~Va can also be used as an external lubricant. External Lubrication: squeeze a small amount (size of a nickel) onto your fingertips and apply to genital area. Vary amount to achieve desired lubrication. ~~To enhance condom use, add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface~~.

Use with Condoms: **For use with condoms apply lubricant directly from tube.** Add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface. For semen collection, only polyurethane condoms should be used.

Change to Internal Package Insert (See ***Appendix L***)

Directions for Using Pre~Va Vaginal Lubricant Externally:
Squeeze a small amount (size of a nickel) onto your fingertips and apply to genital area. Vary amount to achieve desired lubrication. ~~To enhance condom use, add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface.~~

Directions for Using Pre~Va Vaginal Lubricant with Condoms:
For use with condoms apply lubricant directly from tube. Add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface. For semen collection, only polyurethane condoms should be used.

B. Further Justification for Allowing Claims of Compatibility with Latex and Polyurethane Condoms.

1. INGfertility has performed a confirmatory study demonstrating compatibility with the polyurethane condom following lubricant exposure to the applicator (See Section C below and ***Appendix I***).

2. Previously performed condom compatibility studies (latex and polyurethane) were conducted following storage of the lubricant in Dowlex LDPE containers (as described in ***Section 1.b. above***) for 9 months. These data can be viewed in the supplied ***Predicate Binder, Section 3, Condom Compatibility.*** It is unlikely that the LDPE resin used in the applicators would result in condom compatibility different than that found in the original studies. Particularly when the instructions

indicate that the lubricant should not be held in the applicator for any longer than 30 minutes (see revised labeling ***Appendix L***)

C. Summary of Polyurethane Condom Compatibility Testing with Applicator

A condom compatibility study was performed utilizing polyurethane condoms and Pre~Va lubricant exposed to (b)(4) (b)(4) intravaginal applicators for (b)(4) We chose polyurethane condoms, because couples trying to conceive children would most likely use Pre~Va with a condom for semen collection. Polyurethane condoms are appropriate for this use, whereas latex condoms are toxic to sperm and should be avoided in such uses.

This study was performed by (b)(4) (b)(4) the medical device, pharmaceutical and nutraceutical industries. (b)(4) and third-party certified to ISO 9001:2000 and ISO 17025. (b)(4) (b)(4) . The methods, raw data, and findings from this study are shown ***Appendix I***.

Summary of study and results

Pre~Va was exposed to the Intravaginal Applicator comprised of (b)(4) (b)(4) Following this exposure, compatibility testing of the lubricant with polyurethane condoms (b)(4) was performed by (b)(4) in accordance with the United States FDA regulations (21 CFR part 58) for compatibility testing of lubricants with condoms.

Results from this testing are summarized in the Table 1. below and demonstrate that exposure of the lubricant to the applicator for up to (b)(4) does not alter the lubricant's compatibility with polyurethane condoms. Pre~Va in these studies had no statistically significant ($p > 0.05$) effect on condom integrity (tensile strength, elongation at break, or breaking force).

Table 1. Effect of Pre~Va Vaginal Lubricant, Stored for (b)(4) in the (b)(4) Applicator on Polyurethane Condom Compatibility.

Test	Control Condoms (dry)	Condoms Lubricated with Pre~Va	Mean Difference	Mean % Decrease	95% CI	2-sided p-value
Tensile Strength (MPa)	29.84	28.52	-1.33	2.73	±4.92	0.474
Elongation at Break (%)	475.52	465.42	-10.1	1.83	±14.7	0.433
Breaking Force (N)	40.78	38.06	-2.7	1.29	±5.6	0.526

3. Qualitative versus Quantitative assessment of sperm motility*

A. Role of Subjective (Qualitative) Sperm Motility in Human Fertility Assessment

Subjective sperm motility (or referred to by the reviewer as "qualitative") is one of the standard benchmarks in assessing normality of a semen sample. In fact it is a required component of clinical best practice evaluation of male fertility (ASRM, 2006). Subjective motility is most useful in determining the percentage or proportion of motile sperm cells in a sample, as set forth by the WHO and ESHRE guidelines (1999; 2002). For such motility determinations to be accurate, technicians need to conform to CLIA standards, and maintain excellent quality control as referenced. This type of motility assessment is a well defined procedure used across andrology laboratories worldwide. Additionally, it continues to be reported in scientific studies, even when concurrent computer assisted sperm analysis (CASA) is done to report specific motion and velocity outcomes (e.g. Aneck-Hahn et al, 2007). Subjective percent motile sperm correlates well with CASA mean motility, and can allow for more accurate determination of the proportion of motile sperm when debris or other cell types are present.

B. Role of Quantitative (CASA) Sperm Motility in Human Fertility Assessment

CASA allows for quantification of sperm velocity and motion parameters. However normal CASA values for fertile men, and their relationship with pregnancy outcomes, continues to be a topic of debate. Therefore, CASA is viewed clinically as adjunct information and is not part of best practice guidelines for fertility evaluations (ASRM Best Practice Guidelines, 2006). In fact, in one of the few prospective studies evaluating CASA values from a normal population of fertile men, only the percentage of motile sperm was predictive of fertility (p=0.0001),

* See accompanying binder for full references and printed manuscripts

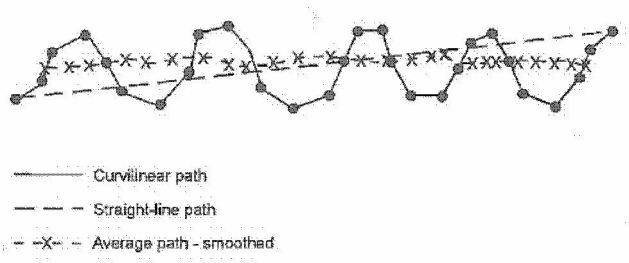
whereas other motion characteristics were not predictive of pregnancy outcomes (Larsen et al. 2000).

In contrast, published guidelines do recognize the value of CASA in reproductive toxicology studies, in particular in lab animal models. CASA motility parameters can change with toxin exposure (ESHRE, 1998; Aneck-Hahn et al, 2007), however, the overall meaning of these changes is not well understood.

One of the challenges with applying CASA to reproductive studies, is that natural fertility requires sperm with motion characteristics relevant to a functional endpoint, such as "good mucus penetrating" kinematics, which are often not measured in this system (Mortimer, 1997; ESHRE 1998; Mortimer, 2002; (b)(4) (b)(4) . More often superiority of samples during CASA is assumed by showing relatively higher velocity of one kind or another.

Specific patterns of sperm motion are required for fertilization, including those observed during cervical mucus penetration (Mortimer, 1997; Mortimer, 2002). Cervical mucus is more viscous than the watery media sperm are often placed in for analysis and ART. Changes in viscosity have a profound impact on the motion of microscopic organisms, including sperm, based on the low Reynolds number environment where they exist (Podolsky & Emlet, 1993; Mortimer 2002). Specifically, current models suggest that sperm in more viscous medium (such as cervical mucus), swim in a straighter line, with a more progressive but somewhat slower path (Mortimer, 1997; Dillon et al., 2007; Wakeley et al., 2007-photo in references). Therefore, sperm motion patterns across environments of different viscosity can not necessarily be compared. Mortimer and Mortimer (1997; 2002; (b)(4) have begun to develop a portrait of sperm with "good" cervical mucus penetrating potential. International bodies have also called for the use of CASA to identify such sperm (ESHRE, 1998). Specifically, these sperm have VAP (average path velocity) of >/= 25 µ/sec, straightness of >/= 80% and ALH (amplitude of lateral head displacement) of >/=2.5 µm, making these sperm linearly progressive to transit the microfiber channels in cervical mucus. This is in contrast to the meandering pathway (VCL) many sperm in a sample may take (Figure 7).

Figure 7. Calculation of the velocities of sperm. The length of each respective path is corrected for distance/time to give the velocity, e.g. the distance traveled along the curvilinear path/s is the curvilinear velocity (VCL), etc. (From S. Mortimer, Human Reproduction Update. 1997)



C. Use of CASA in Pre~Va testing

Both (b)(4) were used in the formula development and initial validation of Pre~Va. Specifically, Pre~Va prototypes were analyzed for motion characteristics using a (b)(4) system. In using CASA for lubricant studies, it is important to note that sperm in control media are in an environment close to (b)(4) whereas sperm with (b)(4)
(b)(4)

I. Methods:

(b)(4)
Data are shown here from semen samples evaluated once the final Pre~Va formulation was established. Specifically, fresh semen samples from men presenting at a local sperm donor bank (b)(4) were used. No lubricants were used during sample collection. Samples were allowed to liquefy and aliquots of raw semen were placed into either the control medium or treated wells (final concentration of (b)(4 Pre~Va in the medium). Semen samples were cultured for (b)(4) Basal medium was (b)(4) Subjective slide motility (to determine percentages of progressively motile sperm) and computer assisted sperm analysis (using an HTM IVOS 12.0) for motion characteristics, were done initially and after culture for (b)(4) in both treatments. Sperm samples in both treatments were also scored as having motion characteristics consistent with "good cervical mucus" penetration potential or not, as noted above (Mortimer, 1997;
(b)(4)

II. Results:

The data from this experiment is provided in ***Appendix J***.

Percent progressively motile sperm did not differ for samples in control medium or with Pre~Va exposure (Figure 8). Sperm exposed to Pre~Va had a higher percent linearity and straightness (Figure 9; $p<0.001$). In contrast, amplitude of lateral head displacement (Figure 10), and curvilinear velocity (Figure 11) were lower ($p < 0.001$) after Pre~Va exposure. Average path velocity and straight line velocity did not differ between the two treatments (Figure 11). Additionally, sperm exposed to Pre~Va had substantially more samples showing "good mucus penetration" potential (Figure 12 ; $p < 0.001$). These results would appear to be consistent with desired sperm motion in a more viscous, but non-toxic environment. Although CASA data can not be transferred across studies, all velocity parameters in both sperm treatments were above the median velocity and motion parameters reported by Larsen et al., 2000 for fertile men from the general population (except for straightness).

While subjective motility has confirmed toxicity of other lubricants in over 10 published studies (see predicate binder), only one such study has published CASA data (Anderson et al., 1998). Specifically, this study showed declines in sperm VCL below 50 µm/sec and VSL below 30 µm/sec after 15 min of exposure to KY lubricant. These values are much lower than the velocity values for sperm exposed to Pre~Va in this study. In contrast, the control velocities (no KY lubricant exposure) in this Anderson study were consistent with the values reported in our data.

Figure 8. Effect of Pre~Va Lubricant on Progressive Sperm Motility

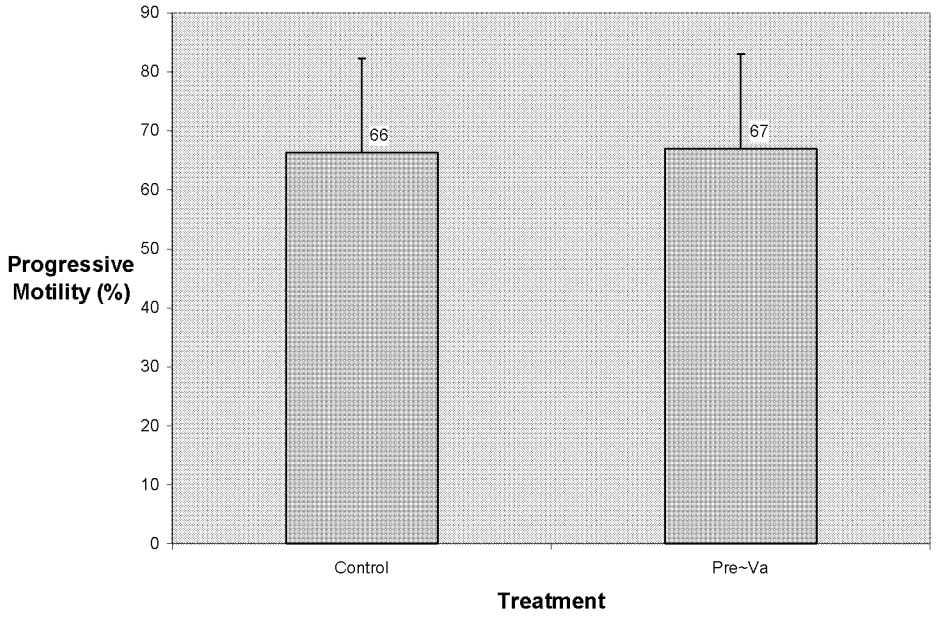


Figure 9. Effect of Pre~Va on Percent Linearity (LIN) and Straightness (STR)

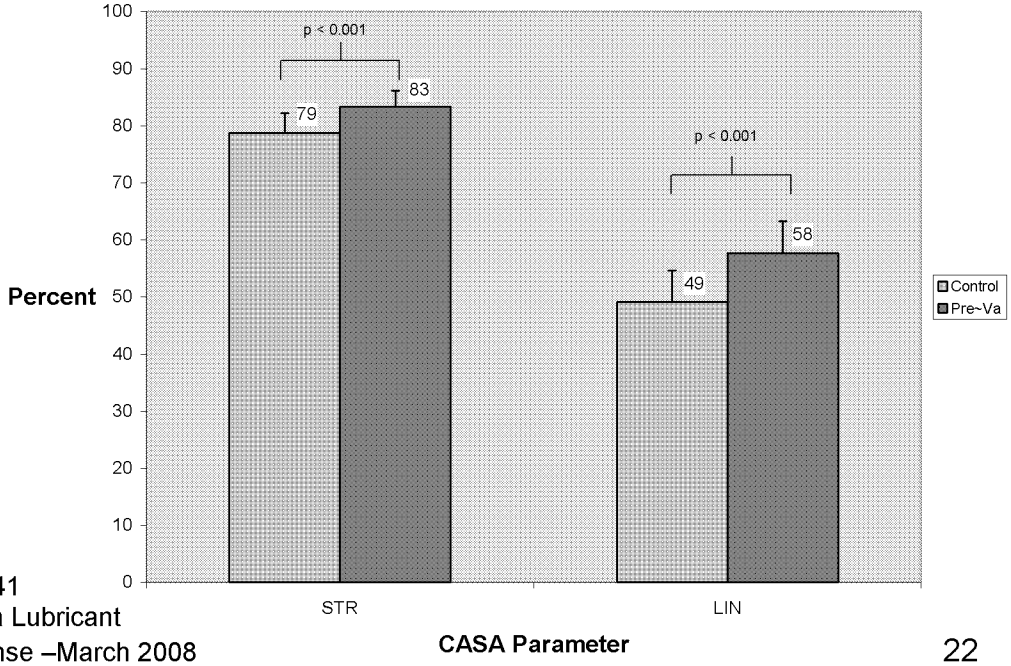


Figure 10. Effect of Pre~Va on Amplitude of Lateral Head Displacement (ALH).

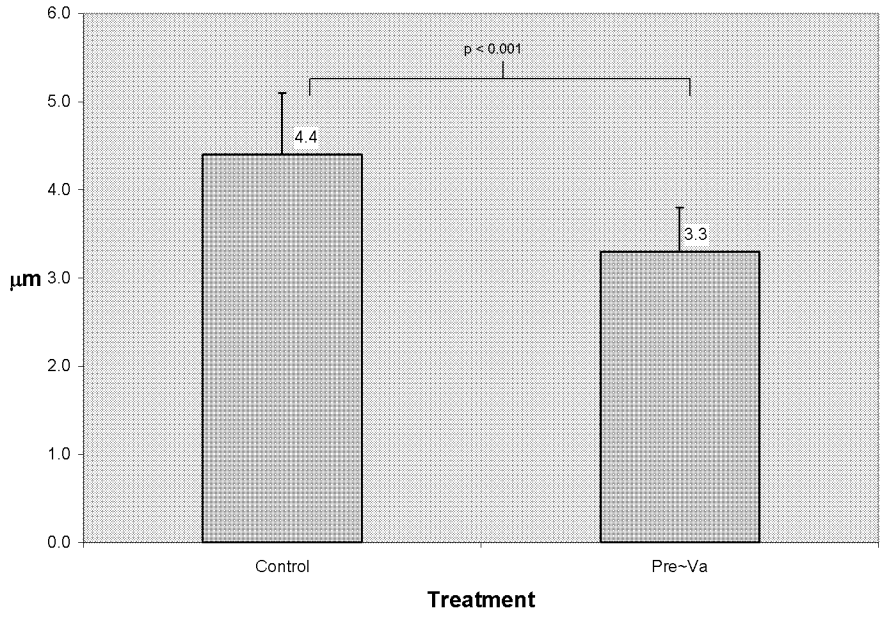


Figure 11. Effect of Pre~Va on Average Path Velocity (VAP), Straight Line Velocity (VSL), and Curvilinear Velocity (VCL).

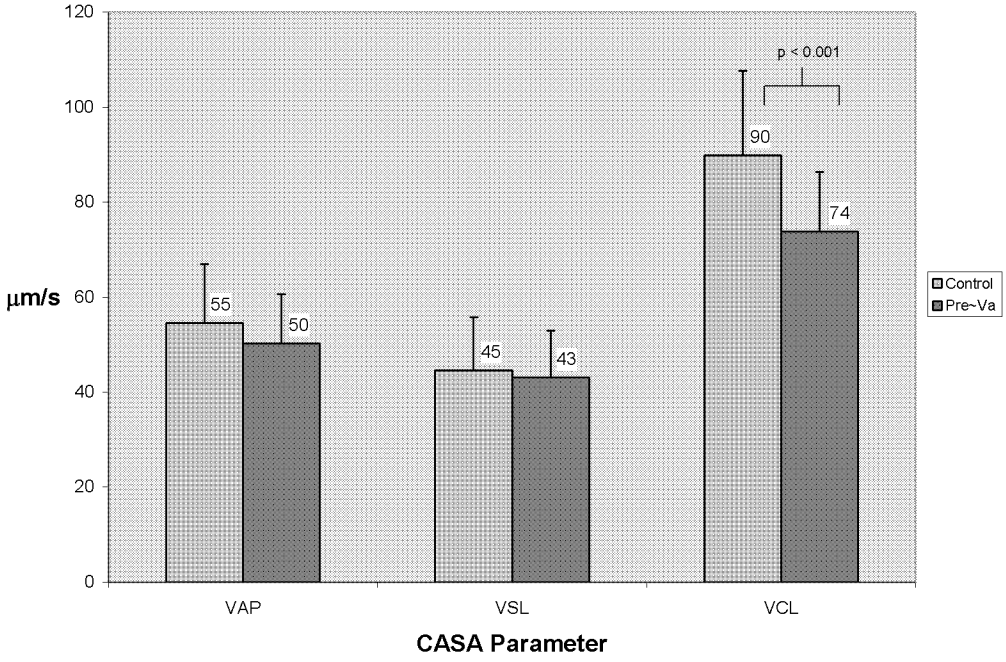
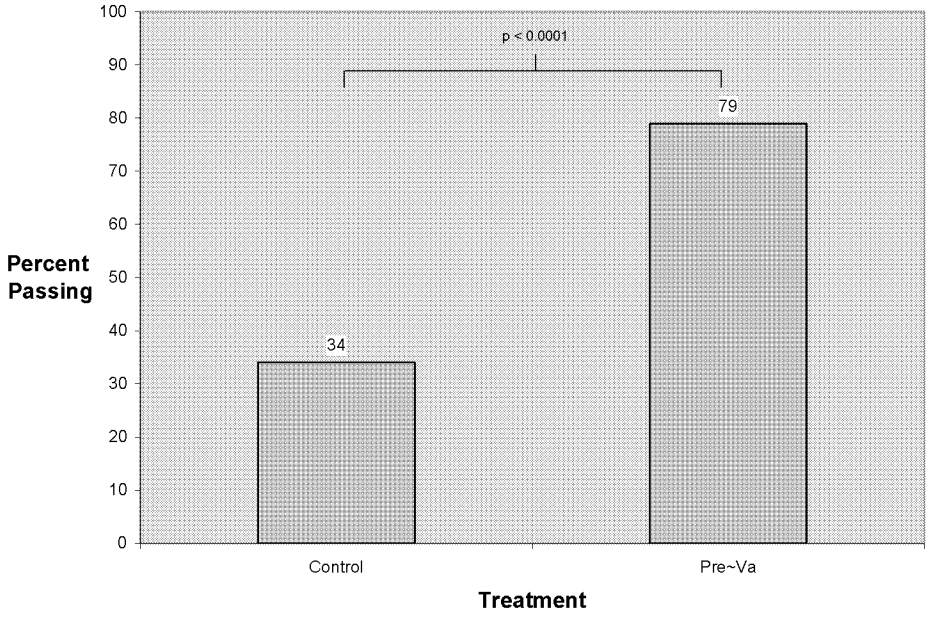


Figure 12. Effect of Pre~Va on Percent of Sperm exhibiting good mucus penetration potential (Percent Passing)



4. Cervical Mucosal Penetration Testing*

A. Rationale for the Bovine Cervical Mucus Penetration Test

We agree with the reviewer that cervical mucus penetration studies offer valuable biocompatibility data. Although INGfertility had performed some limited in-house studies previously, we chose to respond to the reviewer's concern by having a third party evaluate sperm penetration into cervical mucus. The reviewer noted that we could proceed with either postcoital testing (PCT) or an animal cervical mucus model.

The PCT was not used for this evaluation, in part due to its lack of predictive value and sensitivity. Several recent reviews, including the American Society of Reproductive Medicine Practice Guidelines (2006) and Best Practice & Research, Clinical ObGyn (De Sutter, 2006), cite that the PCT,is "obsolete" and that "controversies exist with regards to timing, technique and interpretation" calling its utility and predictive value into "serious question". Other authors cite no difference in pregnancy outcomes at 24 months for couples with abnormal versus normal PCT (Oei et al., 2001). Overall, the reported predictive values for pregnancy achievement associated with an abnormal PCT range from 10-90%, with a specificity ranging from 30-97% (De Sutter, 2006, Montoya , 2002; Oei et al., 1996).

* See accompanying binder for full references and printed manuscripts

(b)(4)

(b)(4) Numerous studies over the years have discussed the use of either human or bovine origin cervical mucus for this assay. Bergman et al., 1981 found excellent correlations between sperm penetration into fresh versus frozen/stored bovine cervical mucus (r=0.985). More importantly Bergman found excellent correlations for sperm penetration into frozen bovine cervical mucus as compared to fresh human cervical mucus (r=0.98). This is because the rheologic and biophysical makeup of human and bovine cervical mucus is similar (discussed in Bergman et al., 1981; Keel & Schalue, 2000).

Human cervical mucus is produced in small volumes, has variable quality in a clinical setting, and is difficult to access. In cattle, large quantities of estrus mucus are produced, making access straightforward, and cows are selected for high fertility, so quality is more consistent. Mucus from several cows can be pooled, frozen stored and subsequently used across an entire experiment, thereby decreasing variability in the assay. In fact, De Geyter et al., 1988 found a better correlation between human IVF outcomes and sperm penetration in bovine cervical mucus, as compared to human cervical mucus, using the end points of vanguard sperm penetration and sperm density at fixed distances. Sharara et al., 1995 found that sperm penetration into human or bovine cervical mucus both correlated with IVF outcomes at a similar rate (r=0.66 respectively). In 2000, Keel & Schalue, performed a large experiment with 1,400 human ejaculates to observe the relationship between ejaculate quality and bovine cervical mucus penetration test (BCMPT) outcomes. They found that sperm motility correlated well with penetration in the BCMPT (r=0.448), in a linear relationship; however, approximately 30% of the samples with normal semen characteristics had abnormal BCMPT. This indicated that the penetration test was evaluating something unique that sperm motion characteristics alone could not detect. Additionally, Sharara et al., 1994 found that BCMPT results for men with normal semen analysis had a 91.5% positive predictive value for their PCT outcomes. This relationship however, dropped for men with abnormal semen analysis to only a 55% positive predictive value.

Most of the references regarding this assay are somewhat dated, due to the increase in sperm injection techniques for treating male factor infertility, and an overall lack of interest (appropriate or not) in cervical mucus physiology. However, a recent article from the agriculture industry where male fertility remains economically relevant, indicated a higher rate of penetration into bovine cervical mucus for cryopreserved sperm from bulls with higher pregnancy rates in cows than that found for sperm from less fertile bulls (Tas et al., 2007). This study confirms the validity of this test. (b)(4)

(b)(4)

B. Bovine Cervical Mucus Penetration Test – Methods and Results

The purpose of this study was to determine whether Pre~Va Vaginal Lubricant has any detrimental effect on sperm penetration into cervical mucus using the Bovine Cervical Mucus Penetration Test. The methods, raw data, and findings from this study are provided in ***Appendix H***.

See ***Section 1.C.IV*** above for a summary of results from the Bovine Cervical Mucus Penetration Test.

C. Conclusion from the Bovine Cervical Mucus Penetration Test

Pre~Va at (b)(4) ***Section 3, Fertility Interventions*** for justification of this test percent), did not inhibit cervical mucus penetration as determined by both the vanguard sperm distance, and sperm density at (b)(4) distances in mucus columns incubated with bull sperm ($p>0.05$). These results provide evidence that the use of Pre~Va vaginal lubricant has no detrimental affect on sperm penetration into cervical mucus.

Biocompatibility

5. Biocompatibility Testing of the Resin Utilized for the Applicator.

A. The safety of the (b)(4) applicator to be marketed with Pre~Va lubricant is supported by information gathered from our vendor. The following information can be found in the referenced appendices.

- ***I.*** Technical data sheets on the resin –(b)(4) ***(Appendix A)***
- ***II.*** A Drug Master File (DMF) access letter for the resin ***(Appendix B)***
- ***III.*** Statement of compliance to California's Proposition 65 ***(Appendix C)***
- ***IV.*** Certification by vendor stating compliance meeting requirements of the Food and Drug Administration 21 CFR, 177.1520 for articles or components intended for use in contact with food. ***(Appendix C)***
- V. Compliance to CONEG Model Legislation regarding heavy metals. ***(Appendix C).***

We request that you consider the information provided in these appendices along with the referenced Drug Master File for evidence that the resin is biocompatible and acceptable for its intended use.

In addition, the manufacturer of the intravaginal applicator, (b)(4) has informed INGfertility that intravaginal applicators comprised of the (b)(4) resin are currently marketed with other approved or cleared products. Specifically, (b)(4) utilizes a similar applicator on their (b)(4) utilizes a similar applicator on their (b)(4) (Personal Communication (b)(4)

B. Cytotoxicity studies of the applicator were performed by (b)(4) (b)(4) utilizing the (b)(4) cell culture assay in triplicate (b)(4) This cytotoxicity test demonstrated NO cytopathic effect of the applicator. The findings of this study are provided in ***Appendix K***.

C. The reviewer stated that "We expect that biocompatibility testing be conducted on the final, sterilized version of the device after exposure to Pre~Va lubricant in accordance with ISO 10993-1…..". Please note that the applicator **will not be sterilized**, nor will any recommendations for sterilization be provided in the labeling (See section 6. below). In fact, we have added language to clarify that the applicator is not sterile, for clinician use.

Sterilization/Packaging/Shelf-life

6. Response to Sterilization/Packaging /Shelf-life Questions

A. Information on Sterilization of Applicators

The applicator will not be provided as a sterilized device and no instructions will be provided for sterilization of the applicator. In the majority of clinic uses and in all home uses of the lubricant, sterilization is not necessary.

There are procedures where the use of a sterilize lubricant may be desired (e.g. intrauterine insemination, embryo transfer). For clarification to the clinician, we have added the following information to the sterilization section of the package insert:

The applicators provided in this package are not sterile. Intravaginal deposition of sterilized lubricant should be performed using a sterile instrument.

Please see ***Appendix L*** for the revised package labeling.

B. Description of how Applicators will be Packaged
Sets of three (3) applicators will be packaged inside of a sealed, clear plastic bag. Two packages of applicators (total of 6) will be provided with each tube of lubricant. The plastic bag will be comprised of (b)(4) (b)(4) Again, the applicators are provided as non-sterile items.

C. Shelf-life of Applicator
The shelf-life for the applicator exceeds the (b)(4) date of the lubricant. Please see ***Appendix O*** for the detailed information regarding shelf-life of the applicator as provided by the vendor.

Indications for Use

7. Statements Regarding "Couples Trying To Conceive" And Use of Applicator

Based on the supportive information provided in this document the following statements are included in the indications for use (see ***Appendices L, M, and N***)

- Pre~Va is safe for use by couples who are trying to conceive.*
- Pre~Va may be deposited intravaginally using the applicator.

> * Please note that this is a slight variance (more grammatically correct) from the previous version requested which was "Pre~Va is safe for use by couples trying to conceive"

8. Modification of Indications for Use Statement

The indications for use statement on the package label (***Appendix L***) has been modified as recommended.

> "Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions."
>
> This statement has also been modified in the Indications for Use Page (***Appendix M***) and the 510(k) summary page (***Appendix N***)

Labeling

9. Clinically Tested and Doctor Recommended Claim

The "Clinically Tested and Doctor Recommended" has been removed from the labeling.

10. Addition of Statement Regarding "DO NOT REUSE APPLICATOR"

The following statement has been added to the packaging label and the package insert (***Appendix L***):

"The applicators are single use only. Dispose of each applicator after use by placing the discarded applicator in a trash receptacle. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand." (please note this is slightly different than the language recommended by the reviewer).

> *"The applicator is single use only. Dispose applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."*

The following statement has been added to the lubricant tube:

"The applicators are single use only. Dispose of each applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand."

11. Storage Conditions Added to Lubricant Tube

The storage conditions have been added to the lubricant tube labeling. In addition, in all of the labeling, room temperature has been defined as 59° to 86°F (***Appendix L***)

(b)(4),Test Data,Test Report

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APPENDIX L

Proposed Labeling
Pre~Va Vaginal Lubricant

PRINCIPAL DISPLAY FRONT
Logo
Pre~Va ™ Vaginal Lubricant
"Fertility~Friendly*" ™

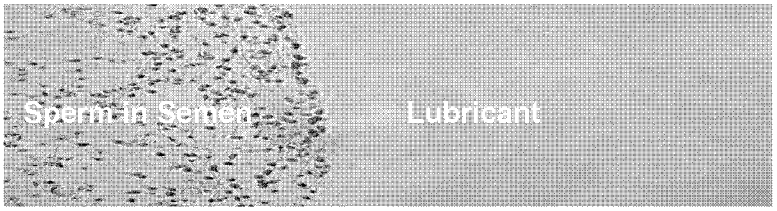
- pH Balanced to Match Fertile Cervical Mucus
- *Uniquely Developed to Not Harm Sperm
- Applicator Coats Vagina with Moisture
- Compatible with latex and polyurethane condoms

With Arabinoglalactan for Antioxidant Support

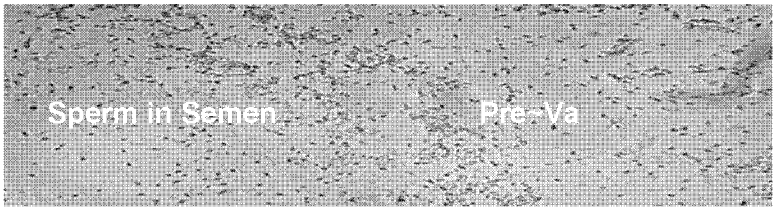
40 gm tube with 6 disposable applicators

PRINCIPAL DISPLAY PANEL BACK AND SIDES
Pre~Va provides moisture without harming sperm. For use even when trying to conceive- a time of increased vaginal dryness* when most other lubricants should be avoided due to their detrimental effects on sperm**.

Popular lubricants can create a barrier that interferes with the ability of swimming sperm to move freely through them.



In contrast, swimming sperm are able to move freely into Pre~Va.*



*Pictures taken in laboratory at 200X magnification after 10 min of contact between semen and products.

Visit www.pre-va.com to view *clinical studies and published studies**.

DIRECTIONS:
Personal Use:
Pre~Va's moisture can best mimic natural secretions, when applied intravaginally. Remove seal from tube opening before initial use. Remove applicator from pouch and twist firmly onto the tube for filling. Fill applicator with the desired amount of Pre~Va, to relieve vaginal dryness. **Do not store lubricant in applicator for more than 30 minutes prior to use**. Insert applicator into vagina to deposit Pre~Va prior to intercourse. See enclosed insert for complete directions and information.

Pre~Va can also be used as an external lubricant. External Lubrication: squeeze a small amount (size of a nickel) onto your fingertips and apply to genital area. Vary amount to achieve desired lubrication.

Use with Condoms: For use with condoms apply lubricant directly from tube, Do Not Use Applicator. Add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface. For semen collection, only polyurethane condoms should be used.

Clinic Use:
Remove seal from tube opening before initial use.

- Applicator: using aseptic technique, fill applicator with desired amount of lubricant and insert into the vagina prior to insertion of instrument. **Do not store lubricant in applicator for more than 30 minutes prior to use.**
- Without Applicator: Using aseptic technique apply desired amount of lubricant to instrument and/or genital area. Vary amount to achieve desired lubrication.

If sterilized product is desired (e.g. intrauterine insemination, embryo transfer) please see package insert for INSTRUCTIONS FOR STERILIZATION. Enclosed applicator is not sterile.

USES: Pre~Va vaginal lubricant supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is

compatible with latex and polyurethane condoms. Pre~Va is also used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.

INGREDIENTS: Purified Water, Hydroxyethylcellulose, Pluronic 127, Sodium Chloride, Sodium Phosphate, Carbopol 934, arabinogalactan, methylparaben, sodium hydroxide, potassium phosphate

Individuals using Pre~Va while trying to conceive:

- Consult your physician if you have not become pregnant following 6-months use of this product.
- No patient data are available regarding viable pregnancies or birth outcomes in patients using this product

Warning: Pre~Va is not a contraceptive. It does not harm sperm or interfere with their function. Keep out of reach of Children.

Caution: If irritation occurs discontinue use immediately, and if it persists consult a physician.

Important:

- The applicators are single use only. Dispose of each applicator after use in a trash receptacle. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand
- Keep cap tightly applied to Pre~Va tube between uses.
- Store at room temperature (59° to 86°F).

QUESTIONS & INFORMATION: Please call us toll-free at 888.471.7333 or visit us at www.ingfertility.com for detailed product information and to review clinical study data*.

Manufactured in the USA for: INGfertility, Valleyford, WA 99036
US Patent #6,593,309 B2

Expiration Date
Lot #

PROPOSED TUBE LABELING
PRE~VA VAGINAL LUBRICANT

PRINCIPAL DISPLAY FRONT
Logo
Pre~Va™ Vaginal Lubricant
"Fertility~Friendly*"

- pH Balanced to Fertile Cervical Mucus
- *Uniquely Developed to Not Harm Sperm
- Applicator Coats Vagina with Moisture

Net Wt. 40 gm tube

Pre~Va provides moisture without harming sperm. For use any time, even while trying to conceive. Learn more & view *clinical studies at www.pre-va.com.

PRINCIPAL DISPLAY BACK & SIDES

DIRECTIONS: See enclosed insert

USES: Pre~Va Lubricant supplements natural lubricating fluids to enhance the ease and comfort of intimate sexual activity. Pre~Va is also used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions.

INGREDIENTS: Purified Water, Hydroxyethylcellulose, Pluronic 127, Sodium Chloride, Sodium Phosphate, Carbopol 934, Arabinogalactan, Methylparaben, Sodium Hydroxide, Potassium Phosphate

IMPORTANT: If the seal on the tube is damaged or opened, DO NOT USE, and return entire contents to place of purchase. The applicators are single use only. Dispose of each applicator after use. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand. Do not store product in applicator for more than 30 minutes prior to use. Store at room temperature (59° to 86°F).

CAUTION: If irritation occurs discontinue use immediately, and if it persists consult a physician.

QUESTIONS: 888.471.7333 or 509.443.0149.

Manufactured in the USA for INGfertility, Valleyford, WA
US Patent #6,593,309 B2

CRIMP OF TUBE: Expiration Date Lot #

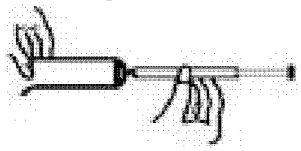
Internal Package Insert

USES: Pre~Va vaginal lubricant supplement the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms. Pre~Va is also used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.

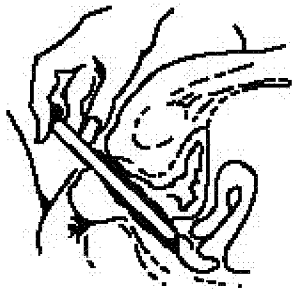
Personal Use

Directions for Using Pre~Va Vaginal Lubricant with Disposable Applicators:

1. Remove seal from tube opening before initial use
2. Pre~Va can be applied up to 15 minutes prior to intercourse. Applying it before you begin making love allows the lubricant to disperse throughout the vagina and allows more spontaneity for you as a couple.
3. Attach the applicator to the tube of lubricant by twisting the end of the applicator firmly onto tube (see picture).



4. Gently squeeze the lubricant into the applicator, continue squeezing until the applicator is full or the desired amount is present in the applicator. Most women will choose the 3 g fill line to meet their product needs. Separate the applicator from the tube. **After each use replace the cap and rollup the tube from the bottom.** Do not leave Pre~Va uncapped between uses.
5. **Do not store lubricant in applicator for more that 30 minutes prior to use.** This means, if you draw Pre~Va into the applicator but do not insert the lubricant intravaginally within 30 minutes, the unused Pre~Va and applicator need to be disposed of.
6. To apply Pre~Va, gently inset the applicator deep into the vagina. This can be done while standing, lying down or sitting (as if on the toilet).
7. Holding the barrel of the applicator, slowly push the plunger all the way in to release the lubricant into the vagina (see picture).



8. Remove both parts of the applicator from the vagina.
9. In order to get the right amount of lubricant for your body, bear down slightly after depositing the product. This will expel any excess Pre~Va that your body doesn't need. If desired, you can then use a tissue to lightly wipe off any product that is on your vulva after application.

Directions for Using Pre~Va Vaginal Lubricant Externally:
Squeeze a small amount (size of a nickel) onto your fingertips and apply to genital area. Vary amount to achieve desired lubrication.

Directions for Using Pre~Va Vaginal Lubricant with Condoms:
For use with condoms apply lubricant directly from tube. Add a small amount of Pre~Va to penis prior to condom use followed by application to outer condom surface. For semen collection, only polyurethane condoms should be used.

Clinic Use:
Remove seal from tube opening before initial use. If sterilized product is desired (e.g. intrauterine insemination, embryo transfer) please see package insert for INSTRUCTIONS FOR STERILIZATION. Enclosed applicators are not sterile and should not be used when sterile product is desired.

With Applicator: Fill one of the enclosed applicators with desired amount of lubricant and insert into the vagina prior to insertion of instrument. **Do not store lubricant in applicator for more than 30 minutes prior to use**.

Without Applicator: Apply desired amount of lubricant to instrument and/or genital area. Vary amount to achieve desired lubrication.

Individuals using Pre~Va while trying to conceive:
- Consult your physician if you have not become pregnant following 6-months use of this product.
- No patient data are available regarding viable pregnancies or birth outcomes in patients using this product

Warning: Pre~Va is not a contraceptive. It does not harm sperm or interfere with their function. Keep out of reach of Children.

Do not use if quality seal on the tube is broken.

Caution: If irritation occurs discontinue use immediately, and if it persists consult a physician.

Important:

- The applicators are single use only. Dispose of each applicator after use by placing the discarded applicator in a trash receptacle. DO NOT REUSE APPLICATOR. If additional lubrication is needed, use a new applicator or apply lubricant by hand
- Store at room temperature (59° to 86°F).

INGREDIENTS: Purified Water, Hydroxyethylcellulose, Pluronic 127, Sodium Chloride, Sodium Phosphate, Carbopol 934, arabinogalactan, methylparaben, sodium hydroxide, potassium phosphate

QUESTIONS & INFORMATION: Please call us toll-free at 888.471.7333 or visit us at www.ingfertility.com for detailed product information and to review clinical study data*.
Manufactured in the USA for: INGfertility, Valleyford, WA 99036
US Patent #6,593,309 B2

QUALITY ASSURANCE

Each lot of Pre~Va Vaginal Lubricant is tested to ensure the following:

Test	**Specification**
pH	7.2-7.45
Osmolarity (ion concentration)	260mOsm-360mOsm
Endotoxin by LAL methodology	< 0.5 EU/ml
Biocompatibility by Mouse Embryo Assay	1-Cell MEA > 80% expanded blastocysts at 96 hours
Biocompatibility by Sperm Motility	Sperm motility after 30-minute exposure to 10% lubricant solution equal to 80% or more that seen for sperm with no lubricant present.

Results of the mouse embryo assay (MEA), endotoxin testing (LAL), and sperm motility assay are reported on a lot specific Certificate of Analysis, which is available upon request.
Expiration Date
Lot #

VALIDATED INSTRUCTIONS FOR STERILIZATION

1. Moist heat/steam sterilization is the preferred and recommended method for Pre~Va Vaginal Lubricant
2. Using aseptic technique transfer desired quantity of lubricant to a steam-compatible container (e.g. conical centrifuge tube of polypropylene or borosilicate glass). Do not fill the container more than 75% capacity to allow room for expansion. Place the cap on the container but do not tighten. The cap must be loose to ensure proper sterilization and to prevent damage to the container.
3. The recommended steam sterilization parameters are as follows:

Sterilizer Type	Temperature	Full Cycle Time
Gravity	121 °C 250 °F	30 minutes

4. Remove the container from the autoclave. Once the container has cooled tighten the cap.
5. Regularly test the efficacy of steam autoclaves as recommended by the equipment manufacturer or local regulations. Sterilizer manufacturer recommendations for operation and load configuration should be followed explicitly.

Important: The applicators provided in this package are not sterile. Intravaginal instillation of sterilized lubricant should be performed using a sterile instrument.

Indications for Use

510(k) Number (if known): K072741

Device Name: Pre~Va Vaginal Lubricant

Indications for Use:

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions.
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms

Prescription Use _____ (Part 21 CFR 801 Subpart D)

AND/OR

Over-The-Counter Use __X_____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

510(k) Summary
Pre~Va Vaginal Lubricant

I. General Information on Submitter

Address:	INGfertility, LLC (Subsidiary of Bio-Origyn, LLC) 17206 S. Spangle Creek Rd. Valleyford, WA 99036 USA
Telephone:	509.443.0149
Fax:	509.471.9638
Email:	dclifton@ingfertility.com
Contact Person:	G. Dennis Clifton, Pharm.D.
Date Prepared:	March 18, 2008

II. General Information on Device

Proprietary Name:	Pre~Va Vaginal Lubricant
Classification Name:	lubricant, patient, vaginal, latex compatible (21 CFR 884.5300, Product Code NUC)

III. Predicate Devices

Predicate Device	510(k) control #
Pre' Vaginal Lubricant	K051436

IV. Description of Device

This product is a non-sterile, water-based personal lubricant formulated to supplement the body's own natural lubricating fluids. Pre~Va is used to lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. It is also used as a personal lubricant to supplement the body's own natural lubricating fluids and to enhance the comfort of intimate sexual activity. The formulation does not harm sperm function and has a pH and osmolarity that are physiologic ("balanced") to that of fertile cervical mucus and semen. The product is compatible with latex and polyurethane condoms. Following is the ingredient list for Pre~Va Vaginal Lubricant:

Ingredients
Water
Hydroxyethylcellulose, NF
Pluronic 127, NF
Sodium Chloride, USP
Arabinogalactan
Sodium Phosphate
Carbopol 934P, NF
Methyl Paraben, USP
Sodium Hydroxide, NF
Potassium Phosphate

V. Intended Use

- To lubricate vaginal tissues to facilitate entry of diagnostic or therapeutic devices including those used in fertility interventions. Pre~Va may be applied directly to the device or may be deposited intravaginally using the applicator, prior to the insertion of diagnostic or therapeutic devices used in fertility interventions
- As a personal lubricant Pre~Va supplements the body's own natural lubricating fluids, to moisturize, relieve friction and to enhance the ease and comfort of intimate sexual activity. Pre~Va is safe for use by couples who are trying to conceive and may be applied to vaginal or penile tissues for lubrication and moisturization purposes. It is compatible with latex and polyurethane condoms.

VI. Technological Characteristics of Device Compared to Predicate Device

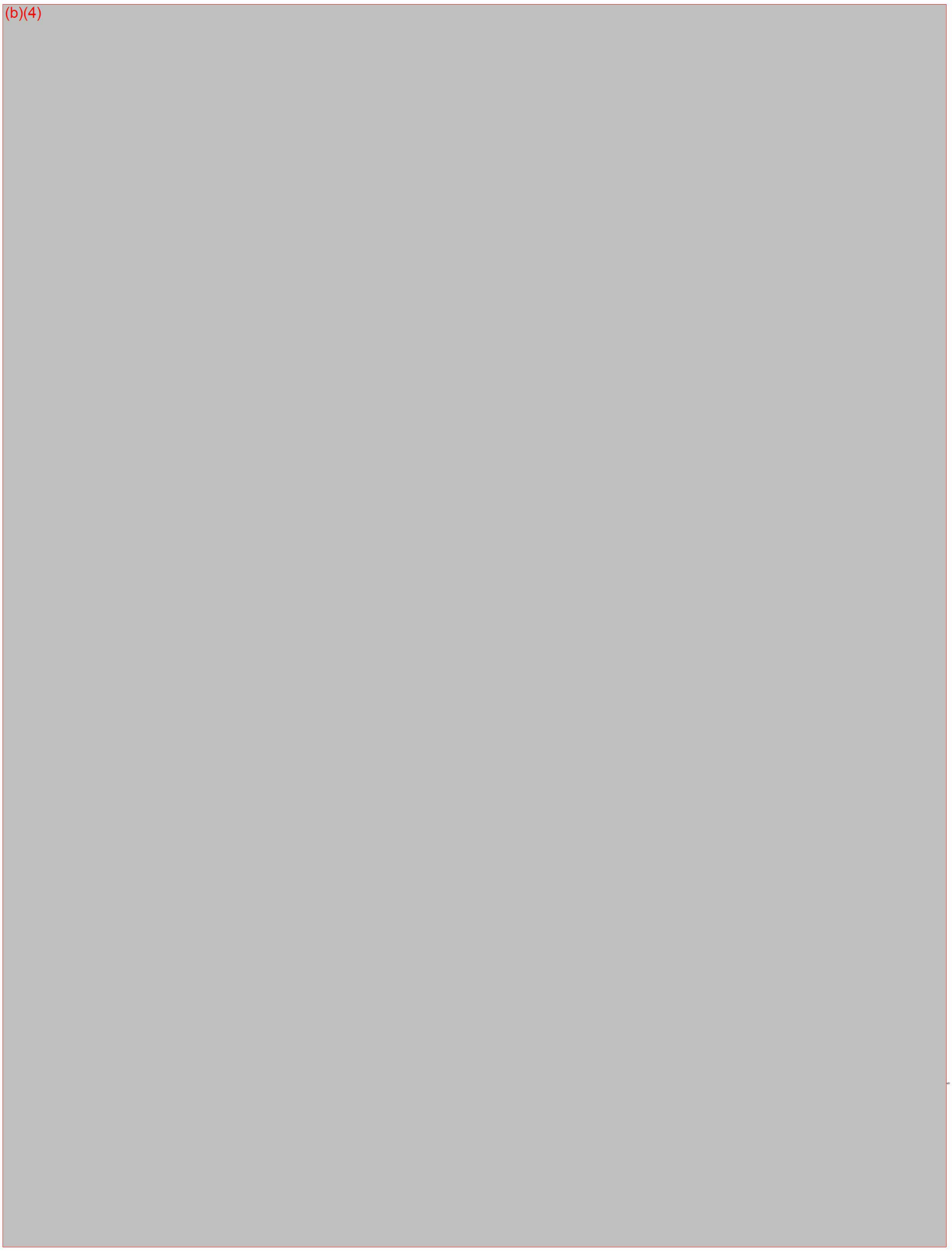
All of the technological characteristics of Pre~Va are identical to the predicate device.

VII. Summary of Performance Data

The performance data of Pre~Va are identical to the predicate.

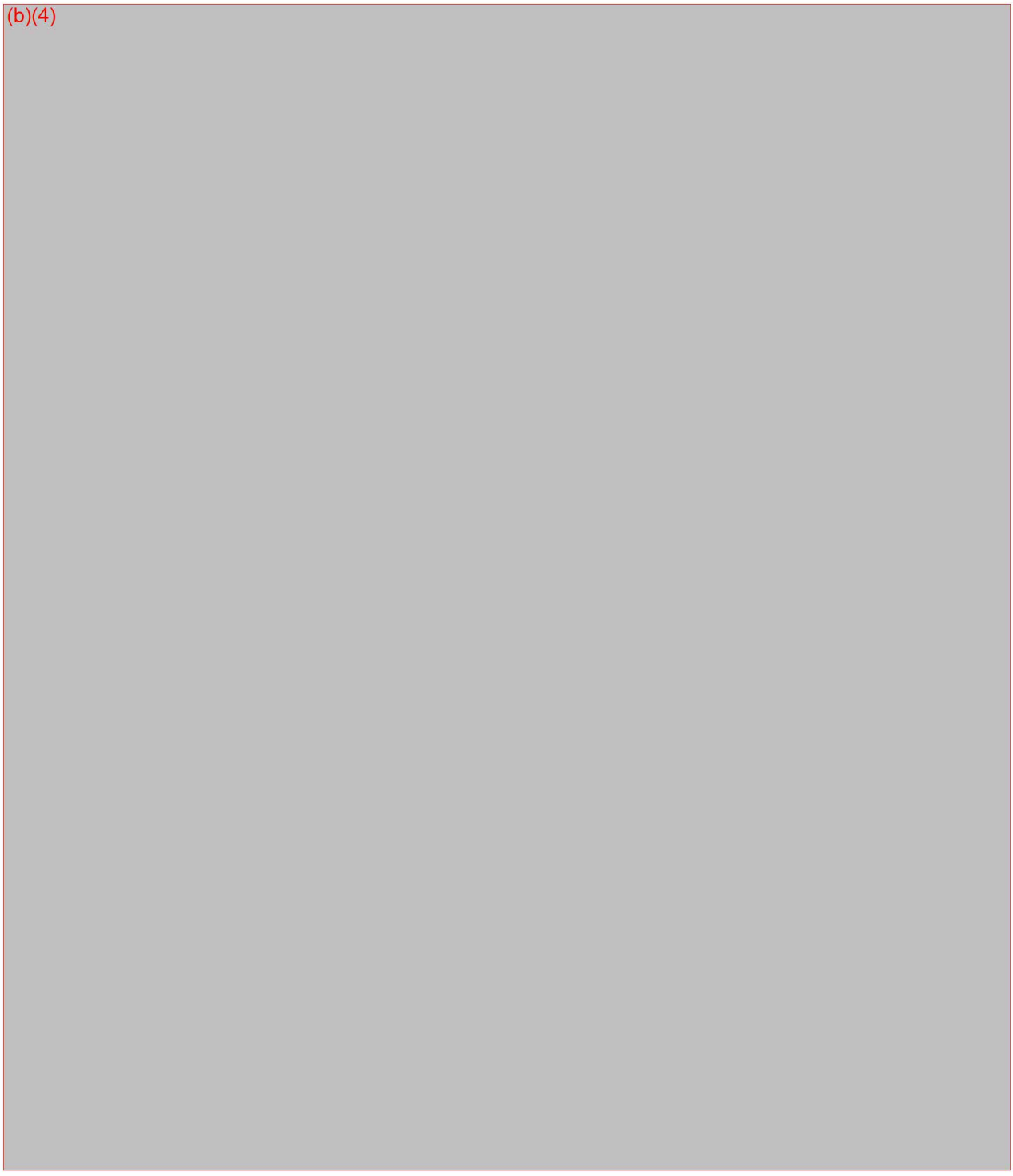
VIII. Conclusion

Pre~Va Vaginal Lubricant is safe for its intended use and substantially equivalent to the predicate device Pre' Vaginal Lubricant.


(b)(4)

Appendix O

(b)(4)



(b)(4)

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Ellington, Joanna E.	Principal Investigator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Vanderbilt University, Nashville			Chemistry
University of Tennessee, Knoxville	DVM	1984	Veterinary Medicine
Cornell University, Ithaca	PhD	1990	Reproductive Physiology

A. Positions and Honors

Positions and Employment

1984-1986 Veterinarian, Briarwood Animal Clinic, Renton, WA
1984-1986 Embryo Transfer Specialist, Bova Transplants, Stanwood, WA
1986-1987 Owner/Veterinarian, Springlake Veterinary Service, Renton, WA
1987-1990 Graduate Research Assistant, Cornell University, Ithaca, NY
1990-1991 Research Associate & Clinical Instructor, Dept. of Clinical Sciences,Cornell University
1992-1994 Theriogenologist, Veterinary Referral Services PS, Spokane, WA
1994-1999 Assist. Professor, College of Vet. Medicine, WSU Spokane, WA
1994-1999 Assistant Professor, College of Pharmacy, WSU Spokane, WA
2000-2003 Director of Biomedical Development, WSU Spokane, WA
2000-2004 Associate Professor, College of Pharmacy, WSU Spokane, WA
1994-present C.E.O., Bio~OriGyn, LLC, ING Fertility, LLC, Spokane, WA
2004-present Associate Professor (Adjunct), College of Pharmacy, WSU Spokane, WA

Other Experience and Professional Memberships

1984 Veterinary Extern, Los Angeles Zoo, Los Angeles, Ca
1984-1986 Embryo Transfer Specialist, Bova Transplants, Stanwood, WA
1984-1986 Veterinarian/Manager, Briarwood Animal Clinic, Renton, WA
Owner/Founder (Equine, Bovine, Swine practice) Springlake Vet. Service Renton, WA
1987-1990 Graduate Research & Teaching Asst., Cornell University, Ithaca, NY
1990 Board Certification, American College of Theriogenologists
1992-2002 Owner/Founder Veterinary Referral Services PS, Spokane, WA

Honors

1988 Kreutter Memorial Award for Bovine Research, Cornell University
1989 Physician Scientist Award NIH training grant, Cornell University
1995 First Independent Research Transition Award NIH, W.S.U.
1999 Nominated for Theriogenologist of the Year
2000-2001 Chair Awards Committee American Society of Andrology
2000-2003 Executive Council American Society of Andrology
2000-2002 USDA NRICGP Review Panel 2001

2002 Co-Chairman Reproductive Toxicology Symposium, Colorado Springs, CO
2003 Young Andrologist Award, American Society of Andrology
2004 Distinguished Alumni Award, College of Veterinary Medicine, University Tennessee

B. Selected peer reviewed publications (selected from 93)

Ball, B.A., Brinsko, S.P., Thomas, P.G., Miller, P.G., & **Ellington, J.E.** Development of 1-2 cell equine embryos to blastocysts after co-culture with oviduct epithelial cells. AJVR 54:1139-1144 (1993).

Ball, B.A., Ignotz, G.G., Brinsko, S.P., Thomas, P.G., Miller, P.G., **Ellington, J.E.** & Currie, W.B. The in vitro block to development and the initiation of transcription in early equine embryos. Equine Vet. Jour. Suppl. 15:87-90 (1993).

Ellington, J.E., Diagnosis, treatment and management of poor fertility in the study dog. Seminars in Vet Med 9:46-53 (1994).

Brinsko, S.P., Ball, B.A., Miller, P.G., Thomas, P.G.A., & **Ellington, J.E.** In vitro development of day two embryos obtained from young, fertile mares and aged subfertile mares. JRF 102:371-378 (1994).

Ellington, J.E., Meyers-Wallen, V.N., & Ball, B.A. Establishment of a co-culture system for canine sperm and oviduct epithelial cells. Vet. Record 136:542-543 (1995).

Brinsko, S.P., Ball, B.A., Ignotz, G.G., Thomas P.G.A., Currie, W.B., & **Ellington, J.E.** Initiation of transcription and nucleologenesis in equine embryos. Mol. Reprod. Dev. 42:298-302 (1995).

Brinsko, S.P., Ball, B.A., & **Ellington, J.E.** In vitro maturation of equine oocytes obtained from different age-groups of sexually mature mares.Theriogenology 44:461-470 (1995).

Samper, J., **Ellington, J.E.**, Burnett, K., Jones, A. & Wright, R. Use of sperm and oviduct cell co-culture as a test for stallion field fertility. Am. Assoc. Equ. Proc., 41:3-5 (1995).

Wright, R.W. & **Ellington, J.E.** Morphological and physiological differences between in vivo and in vitro produced preimplantation embryos from livestock species. Theriogenology 44:1167-1189 (1995).

Stock, A.E., **Ellington, J.E.**, & Fortune, J.E. Superovulatory responses in cattle in the presence vs. absence of a dominant follicle. Theriogenology 45:1091-1102 (1996).

Brinsko, S.P., Ignotz, G., Ball, B., Thomas P., Currie, W., & **Ellington, J.E.** Characterization of polypeptides synthesized and secreted by oviductal epithelial cell explants obtained from young, fertile and aged, subfertile mares. Amer. Jour. Vet. Res. 57:1346-1353 (1996).

Goldman, E., **Ellington, J.E.**, Farrell, P.B. & Foote, R.H. Reaction of fresh and frozen bull spermatozoa incubated with fresh and frozen bovine oviduct epithelial cells. Reprod Dev and Nutr 38:281-288 (1997).

Ellington, J.E., Evenson, D.P., Fleming, J., Rice, G., Brisbois, S., Hiss, G., Wright, R., Jones, A., and Broder, S. Co-culture of human sperm and bovine

Ellington, J.E., Jones, A.E., Davitt, C.M., Schneider, C.S., Brisbois, R.S., Hiss, G.A. and Wright, R.W. Human sperm function in coculture with human, macaque or bovine oviduct epithelial cell monolayers. Hum Reprod. 13:2797-2804 (1998).

Ellington, J.E., Evenson, D.P., Brisbois, R.S., Hiss, G.A., Jones, A.E., Wright, R.W. The higher quality human sperm in a sample selectively attach to oviduct (Fallopian tube) epithelial cells in vitro. Fertil. Steril. 71:924-929 (1999).

Ellington, J.E., Samper, J.C., Jones, A.E., Oliver, S.A., Burnett, K.M., Wright, R.W. Effects of bovine serum albumin on cryopreserved stallion sperm function during media culture and oviduct epithelial cell coculture. Amer. J. Vet. Research 60:363-368 (1999).

Schneider,C., **Ellington, J.E.**, Wright R.W. Effects of bulls with different field fertility on in vitro cleavage and development using sperm coculture systems. Theriogenology 51:1085-1098 (1999).

Ellington, J.E., Samper, J.C., Jones, A.E., Oliver, S.A., Burnett, K.M., Wright, R.W. Interactions of cryopreserved stallion sperm and oviduct epithelial cells or their secretory products in vitro. Animal Reproduction Science, 56:51-65 (1999).

Ellington, J.E., Broemeling, L.D., Broder, S.J. Jones, A.E. Choker, D.A., Wright, R.W. Comparison of fresh and cryopreserved human sperm attachment to bovine oviduct (uterine tube) epithelial cells in vitro. Journal of Andrology, 20:492-499 (1999).

Ellington, J.E. Diagnostic Approaches to Reproductive Toxicology in Animals. Reproductive Toxicology Symposium. August 2002, Colorado Springs, CO.

Bosch P., deAvila J.M., **Ellington, J.E.,** Wright, R.W. Heparin and Ca2+free medium can enhance release of bull sperm attached to oviductal epithelial cell monolayers. Theriogenology 56:247-26 (2001).

Book Chapters:

Ellington, J.E., and Wilker, C.E. Reproductive Toxicology of the Male Companion Animal. In: Small Animal Toxicology, P. Talcott (ed); WB Saunders, (2000; 2005).

Wilker,C.E. and **Ellington, J.E.** Reproductive Toxicology of the Female Companion Animal. In: Small Animal Toxicology, P. Talcott (ed); WB Saunders, (2000; 2005).

Abstracts (selected):

Bosch, P., Ellington, J.E**.,** de Avila, J.M., & Wright, R.W. Ca^{2+}-free medium and heparin can induce release of bull sperm attached to oviductal epithelial cell monolayers. Theriogenology 53:487 (2000).

Ellington J.E., Schneider C.S., Ellington E.J., Broder S.J., Wright R.W. Human sperm function in coculture with and without direct oviduct cell contact. American Society of Andrology, April 2000.

Ellington J.E., Wright R.W., DeAvila J., Jost L.K., Evenson D.P. Sperm chromatin damage reduces blastocyst formation. American Society of Andrology, April 2000.

Ellington J.E., Evenson, D.P., DeAvila J., Jost L.K., Wright R.W. Bull sperm that attach to oviduct cells in vitro support superior embryonic development rates as compared to sperm that do not attach. International Congress on Animal Reproduction, Abstract Volume 1, pp. 78, July 2000.

Samper J.C., **Ellington J.E**., Wright R.W., Jost L.K., Evenson D.P. The effect of extender type, and cold storage or cryopreservation on stallion sperm chromatin structure. International Congress on Animal Reproduction, Stockholm, Abstract Volume 2, pp. 151, July 2000.

Ellington J.E., Samper J.C., Wright R.W. Stallion sperm interactions with oviduct cells in vitro as an indicator of field fertility. International Congress on Animal Reproduction, Stockholm, Abstract Volume 2, pp. 276 Workshop #8, July 2000.

Ellington J.E., Oliver S.A., Evenson D.P. Polysaccharides containing arabinose and galactose decrease oxidative damage of sperm in vitro. American Society of Andrology, VII International Congress on Andrology, Montreal, Canada, abstract accepted, June 15-19, 2001.

Ellington J.E., Oliver S.A., Wright R.W., Samper J.C. Improved stallion sperm function using a plant polysaccharide based sperm wash. American College of Theriogenologists, Vancouver BC, Sept 2001.

Wright RW, Short RA, **Ellington JE.** Effects of personal lubricants on in vitro fertilization and embryo development using a bovine model. American Society of Andrology Annual Meeting, March, 2003; Phoenix, AZ.

Ellington JE, Short RA, Schimmels J Effect of new intimate moisturizer on sperm motility. American Society of Andrology Annual Meeting, March 2003; Phoenix, AZ.

Ellington JE, Daugherty TH, Short RA. Prevalence of vaginal dryness in trying- to-conceive couples. Pacific Coast Reproductive Society Annual Meeting, April 2003; Rancho Mirage, CA.

Ellington, J.E., Schimmels J. The effects of vaginal lubricants on computer assisted sperm analysis parameters associated with cervical mucus penetration. American Society of Reproductive Medicine Annual Meeting, Philadelphia PA, October 2004.

Patents:

Ellington, J.E. and Oliver, S.A. Methods and composition to improve germ cell and embryo function. (US Patents #6140121 and #6593309).

Ellington, J.E. and Oliver, S.A. Use of arabinogalactan in a sperm wash product. (US Patent #5879877).

Oliver, S.A. and **Ellington, J.E.** Use of arabinogalactan in a cell cryopreservation medium. (US Patent #5897987).

Ellington, J.E. and Oliver, S.A. Use of arabinogalactan in cell cryopreservation media (European Patent #87916960.4)
Ellington, J.E. and Oliver, S.A. Use of arabinogalactan in a sperm wash product. (European Patent #97904183.7)
Ellington, J.E. and Oliver, S.A. Composition of arabinogalactan in a sperm wash. (US Patent #6171778)

10 other continuation or international counterparts issued and pending

C. Completed Research Support

1. "Gamete fusion and embryo growth in oviduct cell culture"
   Principal Investigator: J.E. Ellington, DVM, PhD
   Agency: NIH-NICHHD $75,000
   Research Grant Period: 1989-1992
   Type: Physician Scientist Award
2. "Sperm survival and capacitation in oviduct cell cultures"
   Principal Investigator: J.E. Ellington, DVM, PhD
   Agency: NIH-NICHHD (HD 32851) $400,000
   Type: R01 (H09415) Period: April 1, 1995 to March 31, 2000
   The general hypothesis of this proposal is that human sperm can interact with OEC in vitro and undergo biochemical changes, similar to those which occur in the oviduct in vivo; and that differing ability of sperm to undergo these changes in vitro can be used to identify additional categories of male infertility.

3. "Evaluation of stallion sperm survival and capacitation in coculture with mare oviduct cells"
   Principal Investigator: J.E. Ellington, DVM, PhD
   Agency: Grayson-Jockey Club Research Foundation $75,000
   Type: Research Grant Period: September 1, 1994 to August 31, 1996
   The encompassing hypotheses of this proposal are that stallion sperm attach to oviduct epithelial cells (OEC) in vitro and undergo observable biochemical changes, such as capacitation, similar to that seen in the mare; and that the ability of a stallion's sperm to undergo these changes likely relates to his fertility in vivo.

4. "Prototype and Market Assessment of an Improved Storage Medium for Human Platelets".
   Agency: Spokane Intercollegiate Research & Technology Institute $75,000
   Type: Research Grant Period: June 1, 2001 – September 30, 2001
   Due to inferior methods of freezing platelets and inferior methods of storing fresh platelets under short-term conditions, the national blood products industry sustains an annual product loss of nearly $300MM every year. This project was designed to determine a superior prototype for freezing human platelets using a class of proprietary plant sugars to enhance viability and function following cryopreservation.

5. "Molecular Probes of Bull sperm Nuclei Producing Abnormal Embryos."
   Co-Principal Investigator (Don Evenson-PI)
   United States Department of Agriculture 2000-2002 $110,000
   This grant looked at the effects of sperm chromatin damage on subsequent embryo development.

6. "Effects of SSRI Therapy on Sperm Function" Principal Investigator 2000-2002
   Agency: National Institutes of Health. 2000-2002 $145,000
   Type: R 03
   This grant looked at effects of sperm chromatin damage following SSRI (antidepressant) therapy.

7. "Vaginal Gel to Enhance Lubrication and Sperm Function"
   Agency: NICHD 2003-2004, R43 HD4393 $100,000
   Type: SBIR Phase 1
   Phase 1 Development of a novel vaginal gel to enhance sperm-cervical mucus interactions.

DEPARTMENT OF HEALTH AND HUMAN SERVICES Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
Office of Device Evaluation
Document Mail Center (HFZ-401)
9200 Corporate Blvd.
Rockville, Maryland 20850

July 08, 2008

INGFERTILITY, LLC
17206 S. SPANGLE CREEK RD.
VALLEYFORD, WA 99036
ATTN: DENNIS CLIFTON

510(k) Number: K072741
Product: PRE-VA VAGINAL LUBRICANT

The additional information you have submitted has been received.

We will notify you when the processing of this submission has been completed or if any additional information is required. Please remember that all correspondence concerning your submission MUST be sent to the Document Mail Center (HFZ-401) at the above letterhead address. Correspondence sent to any address other than the one above will not be considered as part of your official premarket notification submission. Also, please note the new Blue Book Memorandum regarding Fax and E-mail Policy entitled, "Fax and E-Mail Communication with Industry about Premarket Files Under Review. Please refer to this guidance for information on current fax and e-mail practices at www.fda.gov/cdrh/ode/a02-01.html. On August 12, 2005 CDRH issued the Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s. This guidance can be found at http://www.fda.gov/cdrh/ode/guidance/1567.html. Please refer to this guidance for assistance on how to format an original submission for a Traditional or Abbreviated 510(k).

The Safe Medical Devices Act of 1990, signed on November 28, states that you may not place this device into commercial distribution until you receive a letter from FDA allowing you to do so. As in the past, we intend to complete our review as quickly as possible. Generally we do so in 90 days. However, the complexity of a submission or a requirement for additional information may occasionally cause the review to extend beyond 90 days. Thus, if you have not received a written decision or been contacted within 90 days of our receipt date you may want to check with FDA to determine the status of your submission.

If you have procedural questions, please contact the Division of Small Manufacturers International and Consumer Assistance (DSMICA) at (240)276-3150 or at their toll-free number (800) 638-2041, or contact the 510k staff at (240)276-4040.

Sincerely yours,

Marjorie Shulman
Supervisory Consumer Safety Officer
Premarket Notification Section
Office of Device Evaluation
Center for Devices and
Radiological Health

K072741/S

INGfertility

July 1, 2008

Food and Drug Administration
Center for Devices and Radiological Health
510(k) Document Mail Center (HFZ-401)
9200 Corporate Boulevard
Rockville, MD 20850

FDA CDRH DMC

JUL 08 2008

Received

RE: K072741
Pre~Va Vaginal Lubricant

K-26

Dear Reviewer:

Enclosed with this letter please find the information requested as per your letter of April 25, 2008 with regards to the above referenced 510(k) premarket notification.

The enclosed binder contain the additional information requested to complete the review of our submission.

Thank you in advance for the further review of our application. If you have questions regarding the content of the information provided please contact me at (509) 443-0149 or email dclifton@ingfertility.com.

Sincerely,

G. Dennis Clifton, Pharm.D.
Vice President

17206 Spangle Creek Road
Valleyford, Washington 99036

Voice: 509.443.0149
Toll Free: 888.471.7333
Fax: 509.471.9638
www.ingfertility.com

Table of Contents
Pre~Va Vaginal Lubricant
510(k) Application No. K072741
Response to April 25, 2008 Reviewers Comments

* Sections 1-3 correspond to April 25, 2008 correspondence from Dr. Pollard

Biocompatibility

1. Acute Systemic Toxicity Testing

The reviewer requested that INGfertility provide the results of systemic toxicity testing. This information is necessary to assess if repeated use of this product may cause absorption into the vaginal mucosal tissue and possibly cause systemic effects.

The Acute Systemic Toxicity testing was performed (b)(4) (b)(4) (b)(4) Following are the protocol and results of the Acute Systemic Toxicity.

As the reviewer shall note, Pre~Va, when injected intravenously at (b)(4) normal vaginal dose (gm/Kg basis) demonstrated no acute systemic toxicity. Similarly, when the same amount of Pre~Va was instilled intraperitoneally, no acute systemic toxicity was observed.

A. Dose and Justification of Dose for Acute Systemic Toxicity of Pre~Va Vaginal Lubricant

1. Normal dosing of Pre~Va Lubricant
   The applicator for Pre~Va lubricant is designed to deliver an approximate maximum dose of (b)(4) The graduations on the applicator range from 0.5 to 4 gm. With typical use, Pre~Va will be deposited intravaginally only once per day.

   The (b)(4 maximum dose of Pre~Va lubricant corresponds to approximately (b)(4) based on the median weight of 60Kg for a 25 year old female (NHANES III survey).

   Further Justification of (b) (4) maximum dose
   - Identification of (b) (4) as the maximum dose is further justified based (b)(4) (b)(4)
   - The use of the 60Kg weight is further justified by the fact that the weight of women tend to increase between 25 and 50 years of age. Therefore, the (b)(4) dose represents the upper end of the g/Kg dose in women (for example, the typical maximum dose for a 45 year-old female would be (b)(4)

2. Pre~Va Lubricant dose for Acute Systemic Toxicity Testing
As stated above, the expected maximum dose of Pre~Va lubricant is (b)(4). Traditionally, acute systemic toxicity testing is performed utilizing a dose (b)(4) higher than that of the usual maximum dose. This (b)(4) increased dose is administered to test animals both intravenously and intraperitoneally.

(b)(4) the dose chosen to test the acute systemic toxicity of Pre~Va Lubricant was (b)(4)

B. Protocol and Results for Acute Systemic Toxicity of Pre~Va Vaginal Lubricant

(b)(4),Test protocol,Test Report

(b)(4),Test protocol,Test Report

(b)(4),Test protocol,Test Report

(b)(4),Test protocol,Test Report

(b)(4),Test protocol,Test Report

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(b)(4),Test protocol,Test Report

C. Conclusions and Interpretation from Acute Systemic Toxicity testing of Pre~Va Vaginal Lubricant

Based on the results of the Acute Systemic Toxicity testing, it is concluded that with normal repeated use, systemic toxicity from Pre~Va vaginal lubricant is extremely unlikely. This information, along with the routine biocompatibility data (listed below) and special fertility biocompatibility data (listed below) provides evidence that Pre~Va is safe for the indication for use, "Pre~Va may be deposited intravaginally using the applicator."

Routine Biocompatibility Testing Supporting Safety of Pre~Va

- Rabbit Vaginal Irritation Studies
- Rabbit Penile Irritation Studies
- Human Skin Sensitization Studies
- Slug Mucosal Irritation Test
- Acute Systemic Toxicity Testing

Specialized Fertility Biocompatibility Testing Supporting Safety of Pre~Va

- Effects on Fertilization and Embryo Development
    - Mouse Embryo Assay
    - Bovine in vitro fertilization and embryo development
- Sperm Motility Sperm
- Lubricant Interactions
- Effects on Sperm Chromatin
- Cervical Mucus Penetration

2. Biocompatibility of Applicator to be marketed with Pre~Va Lubricant

A. Additional Information to Establish Biocompatibility

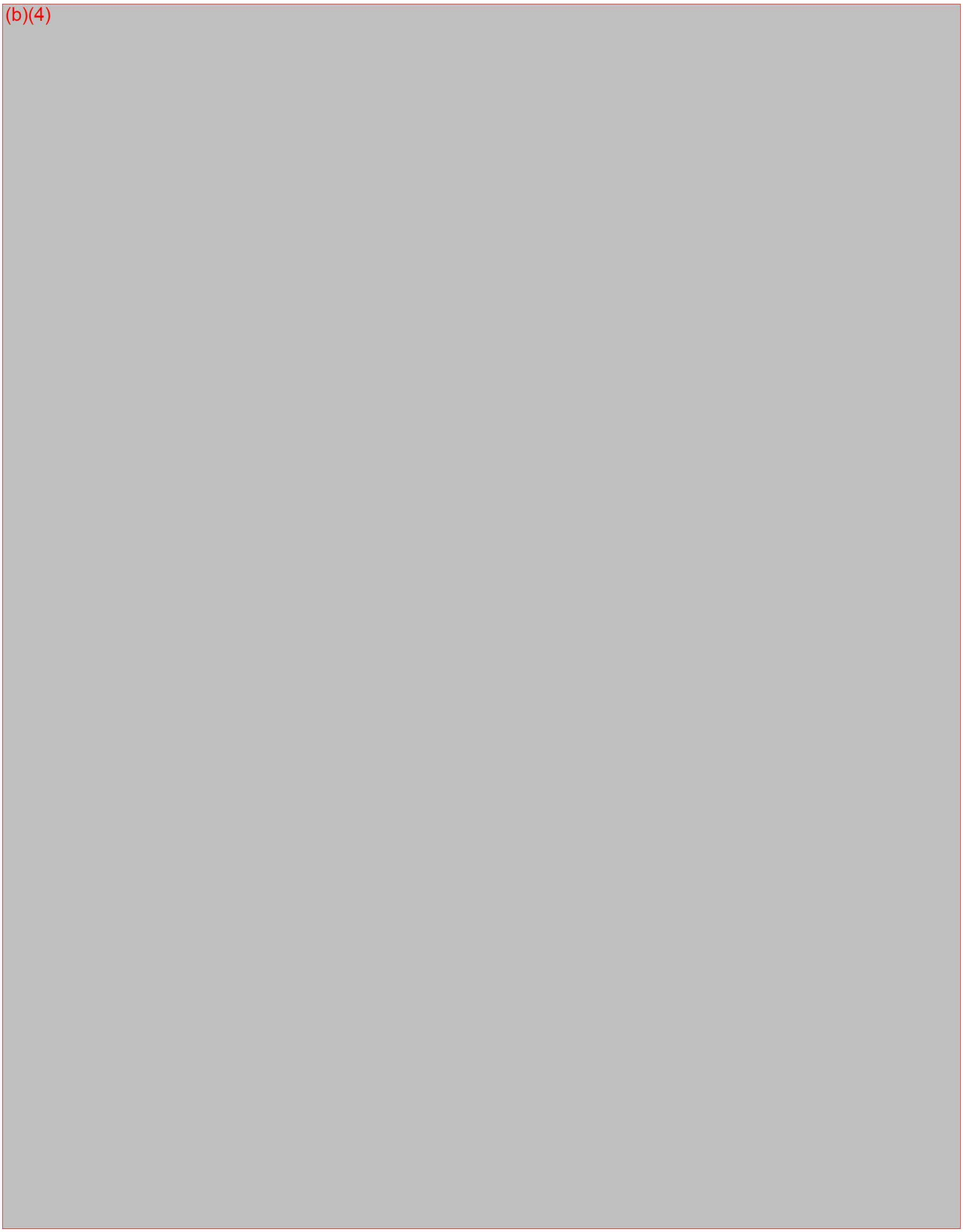
The reviewer stated in the April 2008 response that additional information was necessary to establish the biocompatibility of the applicator for its use with Pre~Va Lubricant. In the response letter INGfertility was given the option to:

a) conduct sensitization and irritation tests, or
b) obtain evidence from the vendor that "the material used for [other products with a similar type and duration of patient contact] is identical to that used for the proposed applicator and has a history of safe use."

In lieu of testing, we have chosen to submit documentation from the applicator vendor, (b)(4) stating that the material used for the proposed applicator is identical to other products with a similar type and duration of patient contact and has a history of safe use.

The following page is a letter from (b)(4) (b)(4) We believe that the evidence provided by (b)(4) substantiates the safety of the applicator for its intended use with Pre~Va Lubricant.

B. Letter from Vendor stating that the material used for other products is identical and has a history of safe use


(b)(4)

Indications for Use

3. The reviewer stated that if INGfertility does not provide sufficient testing or justification to the biocompatibility issues raised (systemic toxicity and applicator safety) we will be asked to remove the following statement from the indications for use, "Pre~Va may be deposited intravaginally using the applicator."

Based on the information provided in Section 1 and Section 2 of this response, INGfertility believes that sufficient testing and justification to the biocompatibility issues raised has been performed and presented. Consequently, the following statement should be included in the indications for use "Pre~Va may be deposited intravaginally using the applicator."